

SEQUENCE LISTING

<110> Lollar, John S.

<120> Nucleic Acid and Amino Acid Sequences
encoding High-Level Expressor Factor VIII Polypeptides and
Methods of Use

<130> 007157/ 276516

<150> PCT/US02/33403
<151> 2002-10-07

<150> 60/327,388
<151> 2001-10-05

<160> 21

<170> FastSEQ for Windows Version 4.0

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Gln Ala Glu Val Tyr Asp Thr Val Val Val Thr Leu Lys Asn Met Ala
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gcg	ata	tca	gac	tca	cag	atc	acg	gcc	tcc	tcc	cac	cta	agc	aat	ata	6000
Ala	Ile	Ser	Asp	Ser	Gln	Ile	Thr	Ala	Ser	Ser	His	Leu	Ser	Asn	Ile	
1985						1990					1995				2000	
ttt	gcc	acc	tgg	tct	cct	tca	caa	gcc	cga	ctt	cac	ctc	cag	ggg	cgg	6048
Phe	Ala	Thr	Trp	Ser	Pro	Ser	Gln	Ala	Arg	Leu	His	Leu	Gln	Gly	Arg	
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acg	aat	gcc	tgg	cga	ccc	cgg	gtg	agc	agc	gca	gag	gag	tgg	ctg	cag	6096
Thr	Asn	Ala	Trp	Arg	Pro	Arg	Val	Ser	Ser	Ala	Glu	Glu	Trp	Leu	Gln	
									2020		2025		2030			
gtg	gac	ctg	cag	aag	acg	gtg	aag	gtc	aca	gca	atc	acc	acc	cag	ggc	6144
Val	Asp	Leu	Gln	Lys	Thr	Val	Lys	Val	Thr	Gly	Ile	Thr	Thr	Gln	Gly	
									2035		2040		2045			
gtg	aag	tcc	ctg	ctc	agc	agc	atg	tat	gtg	aag	gag	ttc	ctc	gtg	tcc	6192
Val	Lys	Ser	Leu	Leu	Ser	Ser	Met	Tyr	Val	Lys	Glu	Phe	Leu	Val	Ser	
									2050		2055		2060			
agt	agt	cag	gac	ggc	cgc	cgc	tgg	acc	ctg	ttt	ctt	cag	gac	ggc	cac	6240
Ser	Ser	Gln	Asp	Gly	Arg	Arg	Trp	Thr	Leu	Phe	Leu	Gln	Asp	Gly	His	
									2065		2070		2075		2080	
acg	aag	gtt	ttt	cag	ggc	aat	cag	gac	tcc	tcc	acc	ccc	gtg	gtg	aac	6288
Thr	Lys	Val	Phe	Gln	Gly	Asn	Gln	Asp	Ser	Ser	Thr	Pro	Val	Val	Asn	
									2085		2090		2095			
gct	ctg	gac	ccc	ccg	ctg	tcc	acg	cgc	tac	ctg	agg	atc	cac	ccc	acg	6336
Ala	Leu	Asp	Pro	Pro	Leu	Phe	Thr	Arg	Tyr	Leu	Arg	Ile	His	Pro	Thr	
									2100		2105		2110			
agc	tgg	gcg	cag	cac	atc	gcc	ctg	agg	ctc	gag	gtt	cta	gga	tgt	gag	6384
Ser	Trp	Ala	Gln	His	Ile	Ala	Leu	Arg	Leu	Glu	Val	Leu	Gly	Cys	Glu	
									2115		2120		2125			
gca	cag	gat	ctc	tac	tga										6402	
Ala	Gln	Asp	Leu	Tyr												
									2130							

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<213> Sus scrofa

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35 40 45
Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val
50 55 60
Leu Tyr Lys Lys Thr Val Phe Val Glu Phe Thr Asp Gln Leu Phe Ser
65 70 75 80
Val Ala Arg Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile
85 90 95
Gln Ala Glu Val Tyr Asp Thr Val Val Val Thr Leu Lys Asn Met Ala
100 105 110
Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Phe Trp Lys Ser
115 120 125

Ser Glu Gly Ala Glu Tyr Glu Asp His Thr Ser Gln Arg Glu Lys Glu
 130 135 140
 Asp Asp Lys Val Leu Pro Gly Lys Ser Gln Thr Tyr Val Trp Gln Val
 145 150 155 160
 Leu Lys Glu Asn Gly Pro Thr Ala Ser Asp Pro Pro Cys Leu Thr Tyr
 165 170 175
 Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu
 180 185 190
 Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Thr Arg Glu Arg
 195 200 205
 Thr Gln Asn Leu His Glu Phe Val Leu Leu Phe Ala Val Phe Asp Glu
 210 215 220
 Gly Lys Ser Trp His Ser Ala Arg Asn Asp Ser Trp Thr Arg Ala Met
 225 230 235 240
 Asp Pro Ala Pro Ala Arg Ala Gln Pro Ala Met His Thr Val Asn Gly
 245 250 255
 Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Lys Lys Ser
 260 265 270
 Val Tyr Trp His Val Ile Gly Met Gly Thr Ser Pro Glu Val His Ser
 275 280 285
 Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg His His Arg Gln Ala
 290 295 300
 Ser Leu Glu Ile Ser Pro Leu Thr Phe Leu Thr Ala Gln Thr Phe Leu
 305 310 315 320
 Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His His
 325 330 335
 His Gly Gly Met Glu Ala His Val Arg Val Glu Ser Cys Ala Glu Glu
 340 345 350
 Pro Gln Leu Arg Arg Lys Ala Asp Glu Glu Asp Tyr Asp Asp Asn
 355 360 365
 Leu Tyr Asp Ser Asp Met Asp Val Val Arg Leu Asp Gly Asp Asp Val
 370 375 380
 Ser Pro Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr
 385 390 395 400
 Trp Val His Tyr Ile Ser Ala Glu Glu Asp Trp Asp Tyr Ala Pro
 405 410 415
 Ala Val Pro Ser Pro Ser Asp Arg Ser Tyr Lys Ser Leu Tyr Leu Asn
 420 425 430
 Ser Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Ala Arg Phe Val
 435 440 445
 Ala Tyr Thr Asp Val Thr Phe Lys Thr Arg Lys Ala Ile Pro Tyr Glu
 450 455 460
 Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu
 465 470 475 480
 Leu Ile Ile Phe Lys Asn Lys Ala Ser Arg Pro Tyr Asn Ile Tyr Pro
 485 490 495
 His Gly Ile Thr Asp Val Ser Ala Leu His Pro Gly Arg Leu Leu Lys
 500 505 510
 Gly Trp Lys His Leu Lys Asp Met Pro Ile Leu Pro Gly Glu Thr Phe
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 Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp
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 Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Ser Ile Asn Leu Glu Lys
 545 550 555 560
 Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu
 565 570 575
 Ser Val Asp Gln Arg Gly Asn Gln Met Met Ser Asp Lys Arg Asn Val
 580 585 590
 Ile Leu Phe Ser Val Phe Asp Glu Asn Gln Ser Trp Tyr Leu Ala Glu
 595 600 605
 Asn Ile Gln Arg Phe Leu Pro Asn Pro Asp Gly Leu Gln Pro Gln Asp
 610 615 620
 Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val
 625 630 635 640
 Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp
 645 650 655

Tyr Ile Leu Ser Val Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe
 660 665 670
 Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr
 675 680 685
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 Gly Leu Trp Val Leu Gly Cys His Asn Ser Asp Leu Arg Asn Arg Gly
 705 710 715 720
 Met Thr Ala Leu Leu Lys Val Tyr Ser Cys Asp Arg Asp Ile Gly Asp
 725 730 735
 Tyr Tyr Asp Asn Thr Tyr Glu Asp Ile Pro Gly Phe Leu Leu Ser Gly
 740 745 750
 Lys Asn Val Ile Glu Pro Arg Ser Phe Ala Gln Asn Ser Arg Pro Pro
 755 760 765
 Ser Ala Ser Gln Lys Gln Phe Gln Thr Ile Thr Ser Pro Glu Asp Asp
 770 775 780
 Val Glu Leu Asp Pro Gln Ser Gly Glu Arg Thr Gln Ala Leu Glu Glu
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 Ala Pro His Gly Ser Ser Ser Asp Leu Gln Glu Ala Arg Asn Glu
 820 825 830
 Ala Asp Asp Tyr Leu Pro Gly Ala Arg Glu Arg Gly Thr Ala Pro Ser
 835 840 845
 Ala Ala Ala Arg Leu Arg Pro Glu Leu His His Ser Ala Glu Arg Val
 850 855 860
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 865 870 875 880
 Ser Ser Ser Asp Leu Leu Lys Thr Ser Pro Thr Ile Pro Ser Asp
 885 890 895
 Thr Leu Ser Ala Glu Thr Glu Arg Thr His Ser Leu Gly Pro Pro His
 900 905 910
 Pro Gln Val Asn Phe Arg Ser Gln Leu Gly Ala Ile Val Leu Gly Lys
 915 920 925
 Asn Ser Ser His Phe Ile Gly Ala Gly Val Pro Leu Gly Ser Thr Glu
 930 935 940
 Glu Asp His Glu Ser Ser Leu Gly Glu Asn Val Ser Pro Val Glu Ser
 945 950 955 960
 Asp Gly Ile Phe Glu Lys Glu Arg Ala His Gly Pro Ala Ser Leu Thr
 965 970 975
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 Lys Ala Arg Val Tyr Leu Lys Thr Asn Arg Lys Ile His Ile Asp Asp
 995 1000 1005
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 Leu Pro Gln Val Tyr Thr Ala Thr Gly Thr Lys Asn Phe Leu Arg Asn
 1140 1145 1150
 Ile Phe His Gln Ser Thr Glu Pro Ser Val Glu Gly Phe Asp Gly Gly
 1155 1160 1165
 Ser His Ala Pro Val Pro Gln Asp Ser Arg Ser Leu Asn Asp Ser Ala
 1170 1175 1180

Glu Arg Ala Glu Thr His Ile Ala His Phe Ser Ala Ile Arg Glu Glu
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 Ala Pro Leu Glu Ala Pro Gly Asn Arg Thr Gly Pro Gly Pro Arg Ser
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 Leu Glu Glu Ile Lys Pro Glu Arg Gly Val Val Leu Asn Ala Thr Ser
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 Thr Arg Trp Ser Glu Ser Pro Ile Leu Gln Gly Ala Lys Arg Asn
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 1285 1290 1295
 Lys Leu Glu Lys Ala Val Leu Ser Ser Ala Gly Leu Ser Glu Ala Ser
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 1315 1320 1325
 Leu Pro Gln Lys Thr Ser Asn Val Ser Cys Ala His Gly Asp Leu Gly
 1330 1335 1340
 Gln Glu Ile Phe Leu Gln Lys Thr Arg Gly Pro Val Asn Leu Asn Lys
 1345 1350 1355 1360
 Val Asn Arg Pro Gly Arg Thr Pro Ser Lys Leu Leu Gly Pro Pro Met
 1365 1370 1375
 Pro Lys Glu Trp Glu Ser Leu Glu Lys Ser Pro Lys Ser Thr Ala Leu
 1380 1385 1390
 Arg Thr Lys Asp Ile Ile Ser Leu Pro Leu Asp Arg His Glu Ser Asn
 1395 1400 1405
 His Ser Ile Ala Ala Lys Asn Glu Gly Gln Ala Glu Thr Gln Arg Glu
 1410 1415 1420
 Ala Ala Trp Thr Lys Gln Gly Gly Pro Gly Arg Leu Cys Ala Pro Lys
 1425 1430 1435 1440
 Pro Pro Val Leu Arg Arg His Gln Arg Asp Ile Ser Leu Pro Thr Phe
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 Gln Pro Glu Glu Asp Lys Met Asp Tyr Asp Asp Ile Phe Ser Thr Glu
 1460 1465 1470
 Thr Lys Gly Glu Asp Phe Asp Ile Tyr Gly Glu Asp Glu Asn Gln Asp
 1475 1480 1485
 Pro Arg Ser Phe Gln Lys Arg Thr Arg His Tyr Phe Ile Ala Ala Val
 1490 1495 1500
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 1540 1545 1550
 Leu Asn Lys His Leu Gly Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val
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 1570 1575 1580
 Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Pro Asp Asp Gln Glu Gln Gly
 1585 1590 1595 1600
 Ala Glu Pro Arg His Asn Phe Val Gln Pro Asn Glu Thr Arg Thr Tyr
 1605 1610 1615
 Phe Trp Lys Val Gln His His Met Ala Pro Thr Glu Asp Glu Phe Asp
 1620 1625 1630
 Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val Asp Leu Glu Lys Asp Val
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 His Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Arg Ala Asn Thr Leu
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 1665 1670 1675 1680
 Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp Tyr Phe Thr Glu Asn Val
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 Glu Arg Asn Cys Arg Ala Pro Cys His Leu Gln Met Glu Asp Pro Thr
 1700 1705 1710

Leu Lys Glu Asn Tyr Arg Phe His Ala Ile Asn Gly Tyr Val Met Asp
 1715 1720 1725
 Thr Leu Pro Gly Leu Val Met Ala Gln Asn Gln Arg Ile Arg Trp Tyr
 1730 1735 1740
 Leu Leu Ser Met Gly Ser Asn Glu Asn Ile His Ser Ile His Phe Ser
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 Gly His Val Phe Ser Val Arg Lys Lys Glu Glu Tyr Lys Met Ala Val
 1765 1770 1775
 Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr Val Glu Met Leu Pro Ser
 1780 1785 1790
 Lys Val Gly Ile Trp Arg Ile Glu Cys Leu Ile Gly Glu His Leu Gln
 1795 1800 1805
 Ala Gly Met Ser Thr Thr Phe Leu Val Tyr Ser Lys Glu Cys Gln Ala
 1810 1815 1820
 Pro Leu Gly Met Ala Ser Gly Arg Ile Arg Asp Phe Gln Ile Thr Ala
 1825 1830 1835 1840
 Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys Leu Ala Arg Leu His Tyr
 1845 1850 1855
 Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys Asp Pro His Ser Trp Ile
 1860 1865 1870
 Lys Val Asp Leu Leu Ala Pro Met Ile Ile His Gly Ile Met Thr Gln
 1875 1880 1885
 Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr Ile Ser Gln Phe Ile Ile
 1890 1895 1900
 Met Tyr Ser Leu Asp Gly Arg Asn Trp Gln Ser Tyr Arg Gly Asn Ser
 1905 1910 1915 1920
 Thr Gly Thr Leu Met Val Phe Phe Gly Asn Val Asp Ala Ser Gly Ile
 1925 1930 1935
 Lys His Asn Ile Phe Asn Pro Pro Ile Val Ala Arg Tyr Ile Arg Leu
 1940 1945 1950
 His Pro Thr His Tyr Ser Ile Arg Ser Thr Leu Arg Met Glu Leu Met
 1955 1960 1965
 Gly Cys Asp Leu Asn Ser Cys Ser Met Pro Leu Gly Met Gln Asn Lys
 1970 1975 1980
 Ala Ile Ser Asp Ser Gln Ile Thr Ala Ser Ser His Leu Ser Asn Ile
 1985 1990 1995 2000
 Phe Ala Thr Trp Ser Pro Ser Gln Ala Arg Leu His Leu Gln Gly Arg
 2005 2010 2015
 Thr Asn Ala Trp Arg Pro Arg Val Ser Ser Ala Glu Glu Trp Leu Gln
 2020 2025 2030
 Val Asp Leu Gln Lys Thr Val Lys Val Thr Gly Ile Thr Thr Gln Gly
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 <223> Factor VIII-- B-domain deleted

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Gly Phe Ser Ala Ile Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser
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tgg gac tac cgg caa agt gaa ctc ctc cgt gag ctg cac gtg gac acc 144
Trp Asp Tyr Arg Gln Ser Glu Leu Leu Arg Glu Leu His Val Asp Thr
35 40 45
aga ttt cct gct aca gcg cca gga gct ctt ccg ttg ggc ccg tca gtc 192
Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val
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ctg tac aaa aag act gtg ttc gta gag ttc acg gat caa ctt ttc agc 240
Leu Tyr Lys Lys Thr Val Phe Val Glu Phe Thr Asp Gln Leu Phe Ser
65 70 75 80
gtt gcc agg ccc agg cca cca tgg atg ggt ctg ctg ggt cct acc atc 288
Val Ala Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile
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cag gct gag gtt tac gac acg gtg gtc gtt acc ctg aag aac atg gct 336
Gln Ala Glu Val Tyr Asp Thr Val Val Val Thr Leu Lys Asn Met Ala
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Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Phe Trp Lys Ser
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Ser Glu Gly Ala Glu Tyr Glu Asp His Thr Ser Gln Arg Glu Lys Glu
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gac gat aaa gtc ctt ccc ggt aaa agc caa acc tac gtc tgg cag gtc 480
Asp Asp Lys Val Leu Pro Gly Lys Ser Gln Thr Tyr Val Trp Gln Val
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ctg aaa gaa aat ggt cca aca gcc tct gac cca cca tgt ctt acc tac 528
Leu Lys Glu Asn Gly Pro Thr Ala Ser Asp Pro Pro Cys Leu Thr Tyr
165 170 175
tca tac ctg tct cac gtg gac ctg gtg aaa gac ctg aat tcg ggc ctc 576
Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu
180 185 190
att gga gcc ctg ctg gtt tgt aga gaa ggg agt ctg acc aga gaa agg 624
Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Thr Arg Glu Arg
195 200 205
acc cag aac ctg cac gaa ttt gta cta ctt ttt gct gtc ttt gat gaa 672
Thr Gln Asn Leu His Glu Phe Val Leu Leu Phe Ala Val Phe Asp Glu
210 215 220
ggg aaa agt tgg cac tca gca aga aat gac tcc tgg aca cgg gcc atg 720
Gly Lys Ser Trp His Ser Ala Arg Asn Asp Ser Trp Thr Arg Ala Met
225 230 235 240
gat ccc gca cct gcc agg gcc cag cct gca atg cac aca gtc aat ggc 768
Asp Pro Ala Pro Ala Arg Ala Gln Pro Ala Met His Thr Val Asn Gly

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tcc ttg gag atc tcg cca cta act ttc ctc act gct cag aca ttc ctg Ser Leu Glu Ile Ser Pro Leu Thr Phe Leu Thr Ala Gln Thr Phe Leu 305 310 315 320			960
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cat ggt ggc atg gag gct cac gtc aga gta gaa agc tgc gcc gag gag His Gly Gly Met Glu Ala His Val Arg Val Glu Ser Cys Ala Glu Glu 340 345 350			1056
ccc cag ctg cgg agg aaa gct gat gaa gag gaa gat tat gat gac aat Pro Gln Leu Arg Arg Lys Ala Asp Glu Glu Asp Tyr Asp Asp Asn 355 360 365			1104
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gcg gtc ccc agc ccc agt gac aga agt tat aaa agt ctc tac ttg aac Ala Val Pro Ser Pro Ser Asp Arg Ser Tyr Lys Ser Leu Tyr Leu Asn 420 425 430			1296
agt ggt cct cag cga att ggt agg aaa tac aaa aaa gct cga ttc gtc Ser Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Ala Arg Phe Val 435 440 445			1344
gct tac acg gat gta aca ttt aag act cgt aaa gct att ccg tat gaa Ala Tyr Thr Asp Val Thr Phe Lys Thr Arg Lys Ala Ile Pro Tyr Glu 450 455 460			1392
tca gga atc ctg gga cct tta ctt tat gga gaa gtt gga gac aca ctt Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu 465 470 475 480			1440
ttg att ata ttt aag aat aaa gcg agc cga cca tat aac atc tac cct Leu Ile Ile Phe Lys Asn Lys Ala Ser Arg Pro Tyr Asn Ile Tyr Pro 485 490 495			1488
cat gga atc act gat gtc agc gct ttg cac cca ggg aga ctt cta aaa His Gly Ile Thr Asp Val Ser Ala Leu His Pro Gly Arg Leu Leu Lys 500 505 510			1536

ggt tgg aaa cat ttg aaa gac atg cca att ctg cca gga gag act ttc Gly Trp Lys His Leu Lys Asp Met Pro Ile Leu Pro Gly Glu Thr Phe 515 520 525	1584
aag tat aaa tgg aca gtg act gtg gaa gat ggg cca acc aag tcc gat Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp 530 535 540	1632
cct cg ^g tgc ctg acc cgc tac tac tcg agc tcc att aat cta gag aaa Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Ile Asn Leu Glu Lys 545 550 555 560	1680
gat ctg gct tcg gga ctc att ggc cct ctc atc tgc tac aaa gaa Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu 565 570 575	1728
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aat att cag cgc ttc ctc ccc aat ccg gat gga tta cag ccc cag gat Asn Ile Gln Arg Phe Leu Pro Asn Pro Asp Gly Leu Gln Pro Gln Asp 610 615 620	1872
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tac att cta agt gtt gga gca cag acg gac ttc ctc tcc gtc ttc ttc Tyr Ile Leu Ser Val Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe 660 665 670	2016
tct ggc tac acc ttc aaa cac aaa atg gtc tat gaa gac aca ctc acc Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr 675 680 685	2064
ctg ttc ccc ttc tca gga gaa acg gtc ttc atg tca atg gaa aac cca Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro 690 695 700	2112
gg ^t ctc tgg gtc ctt ggg tgc cac aac tca gac ttg cgg aac aga ggg Gly Leu Trp Val Leu Gly Cys His Asn Ser Asp Leu Arg Asn Arg Gly 705 710 715 720	2160
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tat tat gac aac act tat gaa gat att cca ggc ttc ttg ctg agt gga Tyr Tyr Asp Asn Thr Tyr Glu Asp Ile Pro Gly Phe Leu Leu Ser Gly 740 745 750	2256
aag aat gtc att gaa cct agg agc ttt gcc cag aat tca aga ccc cct Lys Asn Val Ile Glu Pro Arg Ser Phe Ala Gln Asn Ser Arg Pro Pro 755 760 765	2304
agt gcg agc gct cca aag cct ccg gtc ctg cga cgg cat cag agg gac Ser Ala Ser Ala Pro Lys Pro Pro Val Leu Arg Arg His Gln Arg Asp	2352

770	775	780	
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gag gat gaa aat cag gac cct cgc agc ttt cag aag aga acc cga cac Glu Asp Glu Asn Gln Asp Pro Arg Ser Phe Gln Lys Arg Thr Arg His 820 825 830			2496
tat ttc att gct gcg gtg gag cag ctc tgg gat tac ggg atg agc gaa Tyr Phe Ile Ala Ala Val Glu Gln Leu Trp Asp Tyr Gly Met Ser Glu 835 840 845			2544
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ttc aag aag gtg gtc ttc cgg gaa ttt gct gac ggc tcc ttc acg cag Phe Lys Lys Val Val Phe Arg Glu Phe Ala Asp Gly Ser Phe Thr Gln 865 870 875 880			2640
ccg tcg tac cgc ggg gaa ctc aac aaa cac ttg ggg ctc ttg gga ccc Pro Ser Tyr Arg Gly Glu Leu Asn Lys His Leu Gly Leu Leu Gly Pro 885 890 895			2688
tac atc aga gcg gaa gtt gaa gac aac atc atg gta act ttc aaa aac Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val Thr Phe Lys Asn 900 905 910			2736
cag gcg tct cgt ccc tat tcc ttc tac tcg agc ctt att tct tat ccg Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Pro 915 920 925			2784
gat gat cag gag caa ggg gca gaa cct cga cac aac ttc gtc cag cca Asp Asp Gln Glu Gln Gly Ala Glu Pro Arg His Asn Phe Val Gln Pro 930 935 940			2832
aat gaa acc aga act tac ttt tgg aaa gtg cag cat cac atg gca ccc Asn Glu Thr Arg Thr Tyr Phe Trp Lys Val Gln His His Met Ala Pro 945 950 955 960			2880
aca gaa gac gag ttt gac tgc aaa gcc tgg gcc tac ttt tct gat gtt Thr Glu Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val 965 970 975			2928
gac ctg gaa aaa gat gtg cac tca ggc ttg atc ggc ccc ctt ctg atc Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly Pro Leu Leu Ile 980 985 990			2976
tgc cgc gcc aac acc ctg aac gct gct cac ggt aga caa gtg acc gtg Cys Arg Ala Asn Thr Leu Asn Ala Ala His Gly Arg Gln Val Thr Val 995 1000 1005			3024
caa gaa ttt gct ctg ttt ttc act att ttt gat gag aca aag agc tgg Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp 1010 1015 1020			3072
tac ttc act gaa aat gtg gaa agg aac tgc cgg gcc ccc tgc cat ctg Tyr Phe Thr Glu Asn Val Glu Arg Asn Cys Arg Ala Pro Cys His Leu 1025 1030 1035 1040			3120

cag atg gag gac ccc act ctg aaa gaa aac tat cgc ttc cat gca atc Gln Met Glu Asp Pro Thr Leu Lys Glu Asn Tyr Arg Phe His Ala Ile 1045 1050 1055	3168
aat ggc tat gtg atg gat aca ctc cct ggc tta gta atg gct cag aat Asn Gly Tyr Val Met Asp Thr Leu Pro Gly Leu Val Met Ala Gln Asn 1060 1065 1070	3216
caa agg atc cga tgg tat ctg ctc agc atg ggc agc aat gaa aat atc Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn Ile 1075 1080 1085	3264
cat tcg att cat ttt agc gga cac gtg ttc agt gta cgg aaa aag gag His Ser Ile His Phe Ser Gly His Val Phe Ser Val Arg Lys Lys Glu 1090 1095 1100	3312
gag tat aaa atg gcc gtg tac aat ctc tat ccg ggt gtc ttt gag aca Glu Tyr Lys Met Ala Val Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr 1105 1110 1115 1120	3360
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cac ggc atc atg acc cag ggt gcc cgt cag aag ttt tcc agc ctc tac His Gly Ile Met Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr 1220 1225 1230	3696
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gtg gac gca tct ggg att aaa cac aat att ttt aac cct ccg att gtg Val Asp Ala Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Val 1265 1270 1275 1280	3840
gct cgg tac atc cgt ttg cac cca aca cat tac agc atc cgc agc act Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr 1285 1290 1295	3888
ctt cgc atg gag ttg atg ggc tgt gat tta aac agt tgc agc atg ccc Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro	3936

1300	1305	1310	
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ctt cac ctc cag ggg cgg acg aat gcc tgg cga ccc cgg gtg agc agc Leu His Leu Gln Gly Arg Thr Asn Ala Trp Arg Pro Arg Val Ser Ser 1345	1350	1355	4080
gca gag gag tgg ctg cag gtg gac ctg cag aag acg gtg aag gtc aca Ala Glu Glu Trp Leu Gln Val Asp Leu Gln Lys Thr Val Lys Val Thr 1365	1370	1375	4128
ggc atc acc acc cag ggc gtg aag tcc ctg ctc agc agc atg tat gtg Gly Ile Thr Thr Gln Gly Val Lys Ser Leu Leu Ser Ser Met Tyr Val 1380	1385	1390	4176
aag gag ttc ctc gtg tcc agt agt cag gac ggc cgc cgc tgg acc ctg Lys Glu Phe Leu Val Ser Ser Gln Asp Gly Arg Arg Trp Thr Leu 1395	1400	1405	4224
ttt ctt cag gac ggc cac acg aag gtt ttt cag ggc aat cag gac tcc Phe Leu Gln Asp Gly His Thr Lys Val Phe Gln Gly Asn Gln Asp Ser 1410	1415	1420	4272
tcc acc ccc gtg gtg aac gct ctg gac ccc ccg ctg ttc acg cgc tac Ser Thr Pro Val Val Asn Ala Leu Asp Pro Pro Leu Phe Thr Arg Tyr 1425	1430	1435	4320
ctg agg atc cac ccc acg agc tgg gcg cag cac atc gcc ctg agg ctc Leu Arg Ile His Pro Thr Ser Trp Ala Gln His Ile Ala Leu Arg Leu 1445	1450	1455	4368
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 35 40 45
 Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val
 50 55 60
 Leu Tyr Lys Lys Thr Val Phe Val Glu Phe Thr Asp Gln Leu Phe Ser
 65 70 75 80
 Val Ala Arg Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile
 85 90 95
 Gln Ala Glu Val Tyr Asp Thr Val Val Val Thr Leu Lys Asn Met Ala
 100 105 110
 Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Phe Trp Lys Ser
 115 120 125
 Ser Glu Gly Ala Glu Tyr Glu Asp His Thr Ser Gln Arg Glu Lys Glu

130	135	140
Asp Asp Lys Val Leu Pro Gly Lys Ser Gln Thr Tyr Val Trp Gln Val		
145	150	155 160
Leu Lys Glu Asn Gly Pro Thr Ala Ser Asp Pro Pro Cys Leu Thr Tyr		
165	170	175
Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu		
180	185	190
Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Thr Arg Glu Arg		
195	200	205
Thr Gln Asn Leu His Glu Phe Val Leu Leu Phe Ala Val Phe Asp Glu		
210	215	220
Gly Lys Ser Trp His Ser Ala Arg Asn Asp Ser Trp Thr Arg Ala Met		
225	230	235 240
Asp Pro Ala Pro Ala Arg Ala Gln Pro Ala Met His Thr Val Asn Gly		
245	250	255
Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Lys Lys Ser		
260	265	270
Val Tyr Trp His Val Ile Gly Met Gly Thr Ser Pro Glu Val His Ser		
275	280	285
Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg His His Arg Gln Ala		
290	295	300
Ser Leu Glu Ile Ser Pro Leu Thr Phe Leu Thr Ala Gln Thr Phe Leu		
305	310	315 320
Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His His		
325	330	335
His Gly Gly Met Glu Ala His Val Arg Val Glu Ser Cys Ala Glu Glu		
340	345	350
Pro Gln Leu Arg Arg Lys Ala Asp Glu Glu Glu Asp Tyr Asp Asp Asn		
355	360	365
Leu Tyr Asp Ser Asp Met Asp Val Val Arg Leu Asp Gly Asp Asp Val		
370	375	380
Ser Pro Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr		
385	390	395 400
Trp Val His Tyr Ile Ser Ala Glu Glu Asp Trp Asp Tyr Ala Pro		
405	410	415
Ala Val Pro Ser Pro Ser Asp Arg Ser Tyr Lys Ser Leu Tyr Leu Asn		
420	425	430
Ser Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Ala Arg Phe Val		
435	440	445
Ala Tyr Thr Asp Val Thr Phe Lys Thr Arg Lys Ala Ile Pro Tyr Glu		
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Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu		
465	470	475 480
Leu Ile Ile Phe Lys Asn Lys Ala Ser Arg Pro Tyr Asn Ile Tyr Pro		
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His Gly Ile Thr Asp Val Ser Ala Leu His Pro Gly Arg Leu Leu Lys		
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Gly Trp Lys His Leu Lys Asp Met Pro Ile Leu Pro Gly Glu Thr Phe		
515	520	525
Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp		
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Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Ser Ile Asn Leu Glu Lys		
545	550	555 560
Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu		
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Ser Val Asp Gln Arg Gly Asn Gln Met Met Ser Asp Lys Arg Asn Val		
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Ile Leu Phe Ser Val Phe Asp Glu Asn Gln Ser Trp Tyr Leu Ala Glu		
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Asn Ile Gln Arg Phe Leu Pro Asn Pro Asp Gly Leu Gln Pro Gln Asp		
610	615	620
Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val		
625	630	635 640
Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp		
645	650	655
Tyr Ile Leu Ser Val Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe		

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Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr		
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Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro		
690	695	700
Gly Leu Trp Val Leu Gly Cys His Asn Ser Asp Leu Arg Asn Arg Gly		
705	710	715
Met Thr Ala Leu Leu Lys Val Tyr Ser Cys Asp Arg Asp Ile Gly Asp		
725	730	735
Tyr Tyr Asp Asn Thr Tyr Glu Asp Ile Pro Gly Phe Leu Leu Ser Gly		
740	745	750
Lys Asn Val Ile Glu Pro Arg Ser Phe Ala Gln Asn Ser Arg Pro Pro		
755	760	765
Ser Ala Ser Ala Pro Lys Pro Pro Val Leu Arg Arg His Gln Arg Asp		
770	775	780
Ile Ser Leu Pro Thr Phe Gln Pro Glu Glu Asp Lys Met Asp Tyr Asp		
785	790	795
Asp Ile Phe Ser Thr Glu Thr Lys Gly Glu Asp Phe Asp Ile Tyr Gly		
805	810	815
Glu Asp Glu Asn Gln Asp Pro Arg Ser Phe Gln Lys Arg Thr Arg His		
820	825	830
Tyr Phe Ile Ala Ala Val Glu Gln Leu Trp Asp Tyr Gly Met Ser Glu		
835	840	845
Ser Pro Arg Ala Leu Arg Asn Arg Ala Gln Asn Gly Glu Val Pro Arg		
850	855	860
Phe Lys Lys Val Val Phe Arg Glu Phe Ala Asp Gly Ser Phe Thr Gln		
865	870	875
Pro Ser Tyr Arg Gly Glu Leu Asn Lys His Leu Gly Leu Leu Gly Pro		
885	890	895
Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val Thr Phe Lys Asn		
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Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Pro		
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Asp Asp Gln Glu Gln Gly Ala Glu Pro Arg His Asn Phe Val Gln Pro		
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Asn Glu Thr Arg Thr Tyr Phe Trp Lys Val Gln His His Met Ala Pro		
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Thr Glu Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val		
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Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly Pro Leu Leu Ile		
980	985	990
Cys Arg Ala Asn Thr Leu Asn Ala Ala His Gly Arg Gln Val Thr Val		
995	1000	1005
Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp		
1010	1015	1020
Tyr Phe Thr Glu Asn Val Glu Arg Asn Cys Arg Ala Pro Cys His Leu		
1025	1030	1035
Gln Met Glu Asp Pro Thr Leu Lys Glu Asn Tyr Arg Phe His Ala Ile		
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Asn Gly Tyr Val Met Asp Thr Leu Pro Gly Leu Val Met Ala Gln Asn		
1060	1065	1070
Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn Ile		
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His Ser Ile His Phe Ser Gly His Val Phe Ser Val Arg Lys Lys Glu		
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Glu Tyr Lys Met Ala Val Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr		
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Val Glu Met Leu Pro Ser Lys Val Gly Ile Trp Arg Ile Glu Cys Leu		
1125	1130	1135
Ile Gly Glu His Leu Gln Ala Gly Met Ser Thr Thr Phe Leu Val Tyr		
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Ser Lys Glu Cys Gln Ala Pro Leu Gly Met Ala Ser Gly Arg Ile Arg		
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Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys		
1170	1175	1180
Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys		

1185	1190	1195	1200
Asp Pro His Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile			
1205	1210	1215	
His Gly Ile Met Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr			
1220	1225	1230	
Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Arg Asn Trp Gln			
1235	1240	1245	
Ser Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn			
1250	1255	1260	
Val Asp Ala Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Val			
1265	1270	1275	1280
Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr			
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Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro			
1300	1305	1310	
Leu Gly Met Gln Asn Lys Ala Ile Ser Asp Ser Gln Ile Thr Ala Ser			
1315	1320	1325	
Ser His Leu Ser Asn Ile Phe Ala Thr Trp Ser Pro Ser Gln Ala Arg			
1330	1335	1340	
Leu His Leu Gln Gly Arg Thr Asn Ala Trp Arg Pro Arg Val Ser Ser			
1345	1350	1355	1360
Ala Glu Glu Trp Leu Gln Val Asp Leu Gln Lys Thr Val Lys Val Thr			
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Gly Ile Thr Thr Gln Gly Val Lys Ser Leu Leu Ser Ser Met Tyr Val			
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Lys Glu Phe Leu Val Ser Ser Gln Asp Gly Arg Arg Trp Thr Leu			
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Phe Leu Gln Asp Gly His Thr Lys Val Phe Gln Gly Asn Gln Asp Ser			
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Ser Thr Pro Val Val Asn Ala Leu Asp Pro Pro Leu Phe Thr Arg Tyr			
1425	1430	1435	1440
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ctgtgccttt tgcgattctg ctttagt gcc acc aga aga tac tac ctg ggt gca 234
Ala Thr Arg Arg Tyr Tyr Leu Gly Ala
1 5

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Val Glu Leu Ser Trp Asp Tyr Met Gln Ser Asp Leu Gly Glu Leu Pro
10 15 20 25

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Val Asp Ala Arg Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn
30 35 40

acc tca gtc gtg tac aaa aag act ctg ttt gta gaa ttc acg gtt cac	378
Thr Ser Val Val Tyr Lys Thr Leu Phe Val Glu Phe Thr Val His	
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Leu Phe Asn Ile Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly	
60 65 70	
cct acc atc cag gct gag gtt tat gat aca gtg gtc att aca ctt aag	474
Pro Thr Ile Gln Ala Glu Val Tyr Asp Thr Val Val Ile Thr Leu Lys	
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Asn Met Ala Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr	
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Trp Lys Ala Ser Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg	
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Glu Lys Glu Asp Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val	
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Lys Glu Lys Thr Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val	
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Gln Asp Arg Asp Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr	
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Arg Gln Ala Ser Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln	
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Thr Leu Leu Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser	

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cag ctt gag gat cca gag ttc caa gcc tcc aac atc atg cac agc atc Gln Leu Glu Asp Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile 605 610 615	2058
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aac act ggt gat tat tac gag gac agt tat gaa gat att tca gca tac Asn Thr Gly Asp Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr 715 720 725	2394
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 Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp Asp Lys Val
 115 120 125
 Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu Asn
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 His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser Trp
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 Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn Arg
 225 230 235 240
 Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val Tyr Trp His
 245 250 255
 Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile Phe Leu Glu
 260 265 270
 Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu Glu Ile
 275 280 285
 Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met Asp Leu Gly
 290 295 300
 Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His Asp Gly Met
 305 310 315 320
 Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu Arg
 325 330 335
 Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp Leu Thr Asp
 340 345 350
 Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser Pro Ser Phe
 355 360 365
 Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val His

370	375	380													
Tyr	Ile	Ala	Ala	Glu	Glu	Asp	Trp	Asp	Tyr	Ala	Pro	Leu	Val	Leu	
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Ala	Pro	Asp	Asp	Arg	Ser	Tyr	Lys	Ser	Gln	Tyr	Leu	Asn	Asn	Gly	Pro
				405					410					415	
Gln	Arg	Ile	Gly	Arg	Lys	Tyr	Lys	Lys	Val	Arg	Phe	Met	Ala	Tyr	Thr
				420					425					430	
Asp	Glu	Thr	Phe	Lys	Thr	Arg	Glu	Ala	Ile	Gln	His	Glu	Ser	Gly	Ile
				435				440				445			
Leu	Gly	Pro	Leu	Leu	Tyr	Gly	Glu	Val	Gly	Asp	Thr	Leu	Leu	Ile	Ile
				450				455				460			
Phe	Lys	Asn	Gln	Ala	Ser	Arg	Pro	Tyr	Asn	Ile	Tyr	Pro	His	Gly	Ile
				465				470				475			480
Thr	Asp	Val	Arg	Pro	Leu	Tyr	Ser	Arg	Arg	Leu	Pro	Lys	Gly	Val	Lys
					485					490				495	
His	Leu	Lys	Asp	Phe	Pro	Ile	Leu	Pro	Gly	Glu	Ile	Phe	Lys	Tyr	Lys
					500				505					510	
Trp	Thr	Val	Thr	Val	Glu	Asp	Gly	Pro	Thr	Lys	Ser	Asp	Pro	Arg	Cys
					515				520					525	
Leu	Thr	Arg	Tyr	Tyr	Ser	Ser	Phe	Val	Asn	Met	Glu	Arg	Asp	Leu	Ala
					530				535					540	
Ser	Gly	Leu	Ile	Gly	Pro	Leu	Leu	Ile	Cys	Tyr	Lys	Glu	Ser	Val	Asp
					545				550			555			560
Gln	Arg	Gly	Asn	Gln	Ile	Met	Ser	Asp	Lys	Arg	Asn	Val	Ile	Leu	Phe
					565				570					575	
Ser	Val	Phe	Asp	Glu	Asn	Arg	Ser	Trp	Tyr	Leu	Thr	Glu	Asn	Ile	Gln
					580				585					590	
Arg	Phe	Leu	Pro	Asn	Pro	Ala	Gly	Val	Gln	Leu	Glu	Asp	Pro	Glu	Phe
					595				600					605	
Gln	Ala	Ser	Asn	Ile	Met	His	Ser	Ile	Asn	Gly	Tyr	Val	Phe	Asp	Ser
					610				615					620	
Leu	Gln	Leu	Ser	Val	Cys	Leu	His	Glu	Val	Ala	Tyr	Trp	Tyr	Ile	Leu
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Ser	Ile	Gly	Ala	Gln	Thr	Asp	Phe	Leu	Ser	Val	Phe	Phe	Ser	Gly	Tyr
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Thr	Phe	Lys	His	Lys	Met	Val	Tyr	Glu	Asp	Thr	Leu	Thr	Leu	Phe	Pro
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Phe	Ser	Gly	Glu	Thr	Val	Phe	Met	Ser	Met	Glu	Asn	Pro	Gly	Leu	Trp
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Ile	Leu	Gly	Cys	His	Asn	Ser	Asp	Phe	Arg	Asn	Arg	Gly	Met	Thr	Ala
					690				695					700	
Leu	Leu	Lys	Val	Ser	Ser	Cys	Asp	Lys	Asn	Thr	Gly	Asp	Tyr	Tyr	Glu
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Asp	Ser	Tyr	Glu	Asp	Ile	Ser	Ala	Tyr	Leu	Leu	Ser	Lys	Asn	Asn	Ala
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Ile	Glu	Pro	Arg	Ser	Phe	Ser	Gln	Asn	Ser	Arg	His	Pro	Ser	Thr	Arg
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					755				760					765	
Thr	Asp	Pro	Trp	Phe	Ala	His	Arg	Thr	Pro	Met	Pro	Lys	Ile	Gln	Asn
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Val	Ser	Ser	Ser	Asp	Leu	Leu	Met	Leu	Leu	Arg	Gln	Ser	Pro	Thr	Pro
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Ser	Asp	Asp	Pro	Ser	Pro	Gly	Ala	Ile	Asp	Ser	Asn	Asn	Ser	Leu	Ser
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Glu	Met	Thr	His	Phe	Arg	Pro	Gln	Leu	His	His	Ser	Gly	Asp	Met	Val
					835				840					845	
Phe	Thr	Pro	Glu	Ser	Gly	Leu	Gln	Leu	Arg	Leu	Asn	Glu	Lys	Leu	Gly
					850				855					860	
Thr	Thr	Ala	Ala	Thr	Glu	Leu	Lys	Lys	Leu	Asp	Phe	Lys	Val	Ser	Ser
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Thr	Ser	Asn	Asn	Leu	Ile	Ser	Thr	Ile	Pro	Ser	Asp	Asn	Leu	Ala	Ala
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Tyr Asp Ser Gln Leu Asp Thr Thr	Leu Phe Gly Lys Lys	Ser Ser Pro
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Leu Thr Glu Ser Gly Gly	Pro Leu Ser Leu Ser	Glu Glu Asn Asn Asp
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Ser Lys Leu Leu Glu Ser Gly	Leu Met Asn Ser Gln	Glu Ser Ser Trp
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Gly Lys Asn Val Ser Ser Thr	Glu Ser Gly Arg	Leu Phe Lys Gly Lys
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Arg Ala His Gly Pro Ala Leu Leu	Thr Lys Asp Asn Ala	Leu Phe Lys
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Val Ser Ile Ser Leu Leu Lys	Thr Asn Lys Thr Ser Asn Asn Ser	Ala
995	1000	1005
Thr Asn Arg Lys Thr His Ile	Asp Gly Pro Ser Leu Leu	Ile Glu Asn
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Ser Pro Ser Val Trp Gln Asn Ile	Leu Glu Ser Asp Thr	Glu Phe Lys
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Lys Val Thr Pro Leu Ile His Asp	Arg Met Leu Met Asp	Lys Asn Ala
1045	1050	1055
Thr Ala Leu Arg Leu Asn His	Met Ser Asn Lys	Thr Thr Ser Ser Lys
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Asn Met Glu Met Val Gln Gln	Lys Lys Glu Gly Pro	Ile Pro Pro Asp
1075	1080	1085
Ala Gln Asn Pro Asp Met Ser	Phe Phe Lys Met	Leu Phe Leu Pro Glu
1090	1095	1100
Ser Ala Arg Trp Ile Gln Arg	Thr His Gly Lys Asn	Ser Leu Asn Ser
1105	1110	1115
Gly Gln Gly Pro Ser Pro	Lys Gln Leu Val	Ser Leu Gly Pro Glu Lys
1125	1130	1135
Ser Val Glu Gly Gln Asn Phe	Leu Ser Glu Lys Asn	Lys Val Val Val
1140	1145	1150
Gly Lys Gly Glu Phe Thr Lys	Asp Val Gly Leu Lys	Glu Met Val Phe
1155	1160	1165
Pro Ser Ser Arg Asn Leu Phe	Leu Thr Asn Leu Asp	Asn Leu His Glu
1170	1175	1180
Asn Asn Thr His Asn Gln Glu	Lys Ile Gln Glu Glu	Ile Glu Lys
1185	1190	1195
Lys Glu Thr Leu Ile Gln Glu	Asn Val Val	Leu Pro Gln Ile His Thr
1205	1210	1215
Val Thr Gly Thr Lys Asn Phe	Met Lys Asn Leu Phe	Leu Leu Ser Thr
1220	1225	1230
Arg Gln Asn Val Glu Gly Ser	Tyr Glu Gly Ala	Tyr Ala Pro Val Leu
1235	1240	1245
Gln Asp Phe Arg Ser Leu Asn	Asp Ser Thr Asn Arg	Thr Lys Lys His
1250	1255	1260
Thr Ala His Phe Ser Lys	Gly Glu Glu Asn	Leu Glu Gly Leu
1265	1270	1275
Gly Asn Gln Thr Lys Gln Ile	Val Glu Lys Tyr	Ala Cys Thr Thr Arg
1285	1290	1295
Ile Ser Pro Asn Thr Ser Gln	Gln Asn Phe Val	Thr Gln Arg Ser Lys
1300	1305	1310
Arg Ala Leu Lys Gln Phe	Arg Leu Pro Leu Glu	Glu Thr Glu Leu Glu
1315	1320	1325
Lys Arg Ile Ile Val Asp	Asp Thr Ser Thr	Gln Trp Ser Lys Asn Met
1330	1335	1340
Lys His Leu Thr Pro Ser	Thr Leu Thr Gln Ile	Asp Tyr Asn Glu Lys
1345	1350	1355
Glu Lys Gly Ala Ile Thr	Gln Ser Pro Leu Ser	Asp Cys Leu Thr Arg
1365	1370	1375
Ser His Ser Ile Pro Gln	Ala Asn Arg Ser	Pro Leu Pro Ile Ala Lys
1380	1385	1390
Val Ser Ser Phe Pro Ser	Ile Arg Pro Ile	Tyr Leu Thr Arg Val Leu
1395	1400	1405
Phe Gln Asp Asn Ser Ser	His Leu Pro Ala Ala	Ser Tyr Arg Lys Lys
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Asp Ser Gly Val Gln Glu	Ser Ser His Phe	Leu Gln Gly Ala Lys Lys

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Asn Asn Leu Ser Leu Ala Ile Leu Thr Leu Glu Met Thr Gly Asp Gln			
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Arg Glu Val Gly Ser Leu Gly Thr Ser Ala Thr Asn Ser Val Thr Tyr			
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Lys Lys Val Glu Asn Thr Val Leu Pro Lys Pro Asp Leu Pro Lys Thr			
1475	1480	1485	
Ser Gly Lys Val Glu Leu Leu Pro Lys Val His Ile Tyr Gln Lys Asp			
1490	1495	1500	
Leu Phe Pro Thr Glu Thr Ser Asn Gly Ser Pro Gly His Leu Asp Leu			
1505	1510	1515	1520
Val Glu Gly Ser Leu Leu Gln Gly Thr Glu Gly Ala Ile Lys Trp Asn			
1525	1530	1535	
Glu Ala Asn Arg Pro Gly Lys Val Pro Phe Leu Arg Val Ala Thr Glu			
1540	1545	1550	
Ser Ser Ala Lys Thr Pro Ser Lys Leu Leu Asp Pro Leu Ala Trp Asp			
1555	1560	1565	
Asn His Tyr Gly Thr Gln Ile Pro Lys Glu Glu Trp Lys Ser Gln Glu			
1570	1575	1580	
Lys Ser Pro Glu Lys Thr Ala Phe Lys Lys Asp Thr Ile Leu Ser			
1585	1590	1595	1600
Leu Asn Ala Cys Glu Ser Asn His Ala Ile Ala Ala Ile Asn Glu Gly			
1605	1610	1615	
Gln Asn Lys Pro Glu Ile Glu Val Thr Trp Ala Lys Gln Gly Arg Thr			
1620	1625	1630	
Glu Arg Leu Cys Ser Gln Asn Pro Pro Val Leu Lys Arg His Gln Arg			
1635	1640	1645	
Glu Ile Thr Arg Thr Thr Leu Gln Ser Asp Gln Glu Glu Ile Asp Tyr			
1650	1655	1660	
Asp Asp Thr Ile Ser Val Glu Met Lys Lys Glu Asp Phe Asp Ile Tyr			
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Asp Glu Asp Glu Asn Gln Ser Pro Arg Ser Phe Gln Lys Lys Thr Arg			
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His Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp Asp Tyr Gly Met Ser			
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Ser Ser Pro His Val Leu Arg Asn Arg Ala Gln Ser Gly Ser Val Pro			
1715	1720	1725	
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1745	1750	1755	1760
Pro Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val Thr Phe Arg			
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Asn Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr			
1780	1785	1790	
Glu Glu Asp Gln Arg Gln Gly Ala Glu Pro Arg Lys Asn Phe Val Lys			
1795	1800	1805	
Pro Asn Glu Thr Lys Thr Tyr Phe Trp Lys Val Gln His His Met Ala			
1810	1815	1820	
Pro Thr Lys Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp			
1825	1830	1835	1840
Val Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly Pro Leu Leu			
1845	1850	1855	
Val Cys His Thr Asn Thr Leu Asn Pro Ala His Gly Arg Gln Val Thr			
1860	1865	1870	
Val Gln Glu Phe Ala Leu Phe Thr Ile Phe Asp Glu Thr Lys Ser			
1875	1880	1885	
Trp Tyr Phe Thr Glu Asn Met Glu Arg Asn Cys Arg Ala Pro Cys Asn			
1890	1895	1900	
Ile Gln Met Glu Asp Pro Thr Phe Lys Glu Asn Tyr Arg Phe His Ala			
1905	1910	1915	1920
Ile Asn Gly Tyr Ile Met Asp Thr Leu Pro Gly Leu Val Met Ala Gln			
1925	1930	1935	
Asp Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn			
1940	1945	1950	
Ile His Ser Ile His Phe Ser Gly His Val Phe Thr Val Arg Lys Lys			

1955	1960	1965
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Lys	Met	Ala
Leu	Tyr	Asn
Leu	Tyr	Pro
		Gly
		Val
		Phe
1970	1975	1980
Thr	Val	Glu
Met	Leu	Pro
Leu	Ser	Lys
		Ala
		Gly
1985	1990	1995
Leu	Ile	Gly
Glu	His	Leu
His	Ala	Gly
		Met
		Ser
		Thr
		Leu
		Phe
		Leu
2005	2010	2015
Tyr	Ser	Asn
Lys	Cys	Gln
		Thr
		Pro
		Leu
		Gly
		Met
		Ala
		Ser
		Gly
		His
		Ile
2020	2025	2030
Arg	Asp	Phe
Gln	Ile	Thr
		Ala
		Ser
		Gly
		Gln
		Tyr
		Gly
		Trp
		Ala
2035	2040	2045
Lys	Leu	Ala
Arg	Leu	His
		Tyr
		Ser
		Gly
		Ser
2050	2055	2060
Lys	Glu	Pro
Phe	Ser	Trp
Ile	Lys	Val
		Asp
		Leu
		Leu
		Ala
		Pro
2065	2070	2075
Ile	His	Gly
Ile	Lys	Thr
		Gln
		Gly
		Ala
		Arg
		Gln
		Lys
		Phe
		Ser
		Ser
		Leu
2085	2090	2095
Tyr	Ile	Ser
Gln	Phe	Ile
Ile	Met	Tyr
		Ser
		Leu
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		Gly
		Lys
2100	2105	2110
Gln	Thr	Tyr
Arg	Gly	Asn
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		Thr
		Gly
		Thr
		Leu
		Met
		Val
		Phe
		Phe
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Asn	Val	Asp
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Tyr	Ile	Arg
Leu	His	Pro
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		Tyr
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Pro	Leu	Gly
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		Ile
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Ser	Ser	Tyr
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 <211> 2319
 <212> PRT
 <213> Mus musculus

<400> 8
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 Trp Asn Tyr Ile Gln Ser Asp Leu Leu Ser Val Leu His Thr Asp Ser
 35 40 45
 Arg Phe Leu Pro Arg Met Ser Thr Ser Phe Pro Phe Asn Thr Ser Ile
 50 55 60
 Met Tyr Lys Lys Thr Val Phe Val Glu Tyr Lys Asp Gln Leu Phe Asn
 65 70 75 80
 Ile Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile
 85 90 95

Trp Thr Glu Val His Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala
 100 105 110
 Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala
 115 120 125
 Ser Glu Gly Asp Glu Tyr Glu Asp Gln Thr Ser Gln Met Glu Lys Glu
 130 135 140
 Asp Asp Lys Val Phe Pro Gly Glu Ser His Thr Tyr Val Trp Gln Val
 145 150 155 160
 Leu Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Pro Cys Leu Thr Tyr
 165 170 175
 Ser Tyr Met Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu
 180 185 190
 Ile Gly Ala Leu Leu Val Cys Lys Glu Gly Ser Leu Ser Lys Glu Arg
 195 200 205
 Thr Gln Met Leu Tyr Gln Phe Val Leu Leu Phe Ala Val Phe Asp Glu
 210 215 220
 Gly Lys Ser Trp His Ser Glu Thr Asn Asp Ser Tyr Thr Gln Ser Met
 225 230 235 240
 Asp Ser Ala Ser Ala Arg Asp Trp Pro Lys Met His Thr Val Asn Gly
 245 250 255
 Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser
 260 265 270
 Val Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Ile His Ser
 275 280 285
 Ile Phe Leu Glu Gly His Thr Phe Phe Val Arg Asn His Arg Gln Ala
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 Ser Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu
 305 310 315 320
 Ile Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Lys
 325 330 335
 His Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu
 340 345 350
 Ser Gln Trp Gln Lys Lys Asn Asn Asn Glu Glu Met Glu Asp Tyr Asp
 355 360 365
 Asp Asp Leu Tyr Ser Glu Met Asp Met Phe Thr Leu Asp Tyr Asp Ser
 370 375 380
 Ser Pro Phe Ile Gln Ile Arg Ser Val Ala Lys Lys Tyr Pro Lys Thr
 385 390 395 400
 Trp Ile His Tyr Ile Ser Ala Glu Glu Asp Trp Asp Tyr Ala Pro
 405 410 415
 Ser Val Pro Thr Ser Asp Asn Gly Ser Tyr Lys Ser Gln Tyr Leu Ser
 420 425 430
 Asn Gly Pro His Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Ile
 435 440 445
 Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Thr Ile Gln His Glu
 450 455 460
 Ser Gly Leu Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu
 465 470 475 480
 Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro
 485 490 495
 His Gly Ile Thr Asp Val Ser Pro Leu His Ala Arg Arg Leu Pro Arg
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 Gly Ile Lys His Val Lys Asp Leu Pro Ile His Pro Gly Glu Ile Phe
 515 520 525
 Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp
 530 535 540
 Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Ile Asn Pro Glu Arg
 545 550 555 560
 Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu
 565 570 575
 Ser Val Asp Gln Arg Gly Asn Gln Met Met Ser Asp Lys Arg Asn Val
 580 585 590
 Ile Leu Phe Ser Ile Phe Asp Glu Asn Gln Ser Trp Tyr Ile Thr Glu
 595 600 605
 Asn Met Gln Arg Phe Leu Pro Asn Ala Ala Lys Thr Gln Pro Gln Asp
 610 615 620

Pro Gly Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val
 625 630 635 640
 Phe Asp Ser Leu Glu Leu Thr Val Cys Leu His Glu Val Ala Tyr Trp
 645 650 655
 His Ile Leu Ser Val Gly Ala Gln Thr Asp Phe Leu Ser Ile Phe Phe
 660 665 670
 Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr
 675 680 685
 Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro
 690 695 700
 Gly Leu Trp Val Leu Gly Cys His Asn Ser Asp Phe Arg Lys Arg Gly
 705 710 715 720
 Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Ser Thr Ser Asp
 725 730 735
 Tyr Tyr Glu Glu Ile Tyr Glu Asp Ile Pro Thr Gln Leu Val Asn Glu
 740 745 750
 Asn Asn Val Ile Asp Pro Arg Ser Phe Phe Gln Asn Thr Asn His Pro
 755 760 765
 Asn Thr Arg Lys Lys Lys Phe Lys Asp Ser Thr Ile Pro Lys Asn Asp
 770 775 780
 Met Glu Lys Ile Glu Pro Gln Phe Glu Glu Ile Ala Glu Met Leu Lys
 785 790 795 800
 Val Gln Ser Val Ser Val Ser Asp Met Leu Met Leu Leu Gly Gln Ser
 805 810 815
 His Pro Thr Pro His Gly Leu Phe Leu Ser Asp Gly Gln Glu Ala Ile
 820 825 830
 Tyr Glu Ala Ile His Asp Asp His Ser Pro Asn Ala Ile Asp Ser Asn
 835 840 845
 Glu Gly Pro Ser Lys Val Thr Gln Leu Arg Pro Glu Ser His His Ser
 850 855 860
 Glu Lys Ile Val Phe Thr Pro Gln Pro Gly Leu Gln Leu Arg Ser Asn
 865 870 875 880
 Lys Ser Leu Glu Thr Thr Ile Glu Val Lys Trp Lys Lys Leu Gly Leu
 885 890 895
 Gln Val Ser Ser Leu Pro Ser Asn Leu Met Thr Thr Ile Leu Ser
 900 905 910
 Asp Asn Leu Lys Ala Thr Phe Glu Lys Thr Asp Ser Ser Gly Phe Pro
 915 920 925
 Asp Met Pro Val His Ser Ser Lys Leu Ser Thr Thr Ala Phe Gly
 930 935 940
 Lys Lys Ala Tyr Ser Leu Val Gly Ser His Val Pro Leu Asn Ala Ser
 945 950 955 960
 Glu Glu Asn Ser Asp Ser Asn Ile Leu Asp Ser Thr Leu Met Tyr Ser
 965 970 975
 Gln Glu Ser Leu Pro Arg Asp Asn Ile Leu Ser Ile Glu Asn Asp Arg
 980 985 990
 Leu Leu Arg Glu Lys Arg Phe His Gly Ile Ala Leu Leu Thr Lys Asp
 995 1000 1005
 Asn Thr Leu Phe Lys Asp Asn Val Ser Leu Met Lys Thr Asn Lys Thr
 1010 1015 1020
 Tyr Asn His Ser Thr Thr Asn Glu Lys Leu His Thr Glu Ser Pro Thr
 1025 1030 1035 1040
 Ser Ile Glu Asn Ser Thr Thr Asp Leu Gln Asp Ala Ile Leu Lys Val
 1045 1050 1055
 Asn Ser Glu Ile Gln Glu Val Thr Ala Leu Ile His Asp Gly Thr Leu
 1060 1065 1070
 Leu Gly Lys Asn Ser Thr Tyr Leu Arg Leu Asn His Met Leu Asn Arg
 1075 1080 1085
 Thr Thr Ser Thr Lys Asn Lys Asp Ile Phe His Arg Lys Asp Glu Asp
 1090 1095 1100
 Pro Ile Pro Gln Asp Glu Glu Asn Thr Ile Met Pro Phe Ser Lys Met
 1105 1110 1115 1120
 Leu Phe Leu Ser Glu Ser Ser Asn Trp Phe Lys Lys Thr Asn Gly Asn
 1125 1130 1135
 Asn Ser Leu Asn Ser Glu Gln Glu His Ser Pro Lys Gln Leu Val Tyr
 1140 1145 1150

Leu Met Phe Lys Lys Tyr Val Lys Asn Gln Ser Phe Leu Ser Glu Lys
 1155 1160 1165
 Asn Lys Val Thr Val Glu Gln Asp Gly Phe Thr Lys Asn Ile Gly Leu
 1170 1175 1180
 Lys Asp Met Ala Phe Pro His Asn Met Ser Ile Phe Leu Thr Thr Leu
 1185 1190 1195 1200
 Ser Asn Val His Glu Asn Gly Arg His Asn Gln Glu Lys Asn Ile Gln
 1205 1210 1215
 Glu Glu Ile Glu Lys Glu Ala Leu Ile Glu Glu Lys Val Val Leu Pro
 1220 1225 1230
 Gln Val His Glu Ala Thr Gly Ser Lys Asn Phe Leu Lys Asp Ile Leu
 1235 1240 1245
 Ile Leu Gly Thr Arg Gln Asn Ile Ser Leu Tyr Glu Val His Val Pro
 1250 1255 1260
 Val Leu Gln Asn Ile Thr Ser Ile Asn Asn Ser Thr Asn Thr Val Gln
 1265 1270 1275 1280
 Ile His Met Glu His Phe Phe Lys Arg Arg Lys Asp Lys Glu Thr Asn
 1285 1290 1295
 Ser Glu Gly Leu Val Asn Lys Thr Arg Glu Met Val Lys Asn Tyr Pro
 1300 1305 1310
 Ser Gln Lys Asn Ile Thr Thr Gln Arg Ser Lys Arg Ala Leu Gly Gln
 1315 1320 1325
 Phe Arg Leu Ser Thr Gln Trp Leu Lys Thr Ile Asn Cys Ser Thr Gln
 1330 1335 1340
 Cys Ile Ile Lys Gln Ile Asp His Ser Lys Glu Met Lys Lys Phe Ile
 1345 1350 1355 1360
 Thr Lys Ser Ser Leu Ser Asp Ser Ser Val Ile Lys Ser Thr Thr Gln
 1365 1370 1375
 Thr Asn Ser Ser Asp Ser His Ile Val Lys Thr Ser Ala Phe Pro Pro
 1380 1385 1390
 Ile Asp Leu Lys Arg Ser Pro Phe Gln Asn Lys Phe Ser His Val Gln
 1395 1400 1405
 Ala Ser Ser Tyr Ile Tyr Asp Phe Lys Thr Lys Ser Ser Arg Ile Gln
 1410 1415 1420
 Glu Ser Asn Asn Phe Leu Lys Glu Thr Lys Ile Asn Asn Pro Ser Leu
 1425 1430 1435 1440
 Ala Ile Leu Pro Trp Asn Met Phe Ile Asp Gln Gly Lys Phe Thr Ser
 1445 1450 1455
 Pro Gly Lys Ser Asn Thr Asn Ser Val Thr Tyr Lys Lys Arg Glu Asn
 1460 1465 1470
 Ile Ile Phe Leu Lys Pro Thr Leu Pro Glu Glu Ser Gly Lys Ile Glu
 1475 1480 1485
 Leu Leu Pro Gln Val Ser Ile Gln Glu Glu Glu Ile Leu Pro Thr Glu
 1490 1495 1500
 Thr Ser His Gly Ser Pro Gly His Leu Asn Leu Met Lys Glu Val Phe
 1505 1510 1515 1520
 Leu Gln Lys Ile Gln Gly Pro Thr Lys Trp Asn Lys Ala Lys Arg His
 1525 1530 1535
 Gly Glu Ser Ile Lys Gly Lys Thr Glu Ser Ser Lys Asn Thr Arg Ser
 1540 1545 1550
 Lys Leu Leu Asn His His Ala Trp Asp Tyr His Tyr Ala Ala Gln Ile
 1555 1560 1565
 Pro Lys Asp Met Trp Lys Ser Lys Glu Lys Ser Pro Glu Ile Ile Ser
 1570 1575 1580
 Ile Lys Gln Glu Asp Thr Ile Leu Ser Leu Arg Pro His Gly Asn Ser
 1585 1590 1595 1600
 His Ser Ile Gly Ala Asn Glu Lys Gln Asn Trp Pro Gln Arg Glu Thr
 1605 1610 1615
 Thr Trp Val Lys Gln Gly Gln Thr Gln Arg Thr Cys Ser Gln Ile Pro
 1620 1625 1630
 Pro Val Leu Lys Arg His Gln Arg Glu Leu Ser Ala Phe Gln Ser Glu
 1635 1640 1645
 Gln Glu Ala Thr Asp Tyr Asp Asp Ala Ile Thr Ile Glu Thr Ile Glu
 1650 1655 1660
 Asp Phe Asp Ile Tyr Ser Glu Asp Ile Lys Gln Gly Pro Arg Ser Phe
 1665 1670 1675 1680

Gln Gln Lys Thr Arg His Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp
 1685 1690 1695
 Asp Tyr Gly Met Ser Thr Ser His Val Leu Arg Asn Arg Tyr Gln Ser
 1700 1705 1710
 Asp Asn Val Pro Gln Phe Lys Lys Val Val Phe Gln Glu Phe Thr Asp
 1715 1720 1725
 Gly Ser Phe Ser Gln Pro Leu Tyr Arg Gly Glu Leu Asn Glu His Leu
 1730 1735 1740
 Gly Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met
 1745 1750 1755 1760
 Val Thr Phe Lys Asn Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser
 1765 1770 1775
 Leu Ile Ser Tyr Lys Glu Asp Gln Arg Gly Glu Glu Pro Arg Arg Asn
 1780 1785 1790
 Phe Val Lys Pro Asn Glu Thr Lys Ile Tyr Phe Trp Lys Val Gln His
 1795 1800 1805
 His Met Ala Pro Thr Glu Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr
 1810 1815 1820
 Phe Ser Asp Val Asp Leu Glu Arg Asp Met His Ser Gly Leu Ile Gly
 1825 1830 1835 1840
 Pro Leu Leu Ile Cys His Ala Asn Thr Leu Asn Pro Ala His Gly Arg
 1845 1850 1855
 Gln Val Ser Val Gln Glu Phe Ala Leu Leu Phe Thr Ile Phe Asp Glu
 1860 1865 1870
 Thr Lys Ser Trp Tyr Phe Thr Glu Asn Val Lys Arg Asn Cys Lys Thr
 1875 1880 1885
 Pro Cys Asn Phe Gln Met Glu Asp Pro Thr Leu Lys Glu Asn Tyr Arg
 1890 1895 1900
 Phe His Ala Ile Asn Gly Tyr Val Met Asp Thr Leu Pro Gly Leu Val
 1905 1910 1915 1920
 Met Ala Gln Asp Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Asn
 1925 1930 1935
 Asn Glu Asn Ile Gln Ser Ile His Phe Ser Gly His Val Phe Thr Val
 1940 1945 1950
 Arg Lys Lys Glu Glu Tyr Lys Met Ala Val Tyr Asn Leu Tyr Pro Gly
 1955 1960 1965
 Val Phe Glu Thr Leu Glu Met Ile Pro Ser Arg Ala Gly Ile Trp Arg
 1970 1975 1980
 Val Glu Cys Leu Ile Gly Glu His Leu Gln Ala Gly Met Ser Thr Leu
 1985 1990 1995 2000
 Phe Leu Val Tyr Ser Lys Gln Cys Gln Ile Pro Leu Gly Met Ala Ser
 2005 2010 2015
 Gly Ser Ile Arg Asp Phe Gln Ile Thr Ala Ser Gly His Tyr Gly Gln
 2020 2025 2030
 Trp Ala Pro Asn Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala
 2035 2040 2045
 Trp Ser Thr Lys Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala
 2050 2055 2060
 Pro Met Ile Val His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe
 2065 2070 2075 2080
 Ser Ser Leu Tyr Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly
 2085 2090 2095
 Lys Lys Trp Leu Ser Tyr Gln Gly Asn Ser Thr Gly Thr Leu Met Val
 2100 2105 2110
 Phe Phe Gly Asn Val Asp Ser Ser Gly Ile Lys His Asn Ser Phe Asn
 2115 2120 2125
 Pro Pro Ile Ile Ala Arg Tyr Ile Arg Leu His Pro Thr His Ser Ser
 2130 2135 2140
 Ile Arg Ser Thr Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser
 2145 2150 2155 2160
 Cys Ser Ile Pro Leu Gly Met Glu Ser Lys Val Ile Ser Asp Thr Gln
 2165 2170 2175
 Ile Thr Ala Ser Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro
 2180 2185 2190
 Ser Gln Ala Arg Leu His Leu Gln Gly Arg Thr Asn Ala Trp Arg Pro
 2195 2200 2205

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Gln Val Asn Asp Pro Lys Gln Trp Leu Gln Val Asp Leu Gln Lys Thr
2210          2215          2220
Met Lys Val Thr Gly Ile Ile Thr Gln Gly Val Lys Ser Leu Phe Thr
2225          2230          2235          2240
Ser Met Phe Val Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His
2245          2250          2255
His Trp Thr Gln Ile Leu Tyr Asn Gly Lys Val Lys Val Phe Gln Gly
2260          2265          2270
Asn Gln Asp Ser Ser Thr Pro Met Met Asn Ser Leu Asp Pro Pro Leu
2275          2280          2285
Leu Thr Arg Tyr Leu Arg Ile His Pro Gln Ile Trp Glu His Gln Ile
2290          2295          2300
Ala Leu Arg Leu Glu Ile Leu Gly Cys Glu Ala Gln Gln Gln Tyr
2305          2310          2315

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<210> 9
<211> 14
<212> PRT
<213> Homo sapeins

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<220>
<221> DOMAIN
<222> (1)...(14)
<223> Linker sequence

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Ser Phe Ser Gln Asn Pro Pro Val Leu Lys Arg His Gln Arg
1          5          10

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<210> 10
<211> 4
<212> PRT
<213> Homo sapiens

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<400> 10
Arg His Gln Arg
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<210> 11
<211> 24
<212> PRT
<213> Sus Scrofa

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<220>
<221> DOMAIN
<222> (1)...(24)
<223> Linker sequence

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<400> 11
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Pro Val Leu Arg Arg His Gln Arg
20

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<210> 12
<211> 4371
<212> DNA
<213> Homo sapiens

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<220>
<221> CDS

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<222> (1)...(4371)
 <223> B domain-deleted factor VIII
 (HSQ)

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Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe				.
1	5	10	15	.
tgc ttt agt gcc acc aga aga tac tac ctg ggt gca gtg gaa ctg tca				96
Cys Phe Ser Ala Thr Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser				.
20	25	30		.
tgg gac tat atg caa agt gat ctc ggt gag ctg cct gtg gac gca aga				144
Trp Asp Tyr Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg				.
35	40	45		.
ttt cct cct aga gtg cca aaa tct ttt cca ttc aac acc tca gtc gtg				192
Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val				.
50	55	60		.
tac aaa aag act ctg ttt gta gaa ttc acg gtt cac ctt ttc aac atc				240
Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Val His Leu Phe Asn Ile				.
65	70	75	80	.
gct aag cca agg cca ccc tgg atg ggt ctg cta ggt cct acc atc cag				288
Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln				.
85	90	95		.
gct gag gtt tat gat aca gtg gtc att aca ctt aag aac atg gct tcc				336
Ala Glu Val Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser				.
100	105	110		.
cat cct gtc agt ctt cat gct gtt gta tcc tac tgg aaa gct tct				384
His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser				.
115	120	125		.
gag gga gct gaa tat gat gat cag acc agt caa agg gag aaa gaa gat				432
Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp				.
130	135	140		.
gat aaa gtc ttc cct ggt gga agc cat aca tat gtc tgg cag gtc ctg				480
Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu				.
145	150	155	160	.
aaa gag aat ggt cca atg gcc tct gac cca ctg tgc ctt acc tac tca				528
Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser				.
165	170	175		.
tat ctt tct cat gtg gac ctg gta aaa gac ttg aat tca ggc ctc att				576
Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile				.
180	185	190		.
gga gcc cta cta gta tgt aga gaa ggg agt ctg gcc aag gaa aag aca				624
Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr				.
195	200	205		.
cag acc ttg cac aaa ttt ata cta ctt ttt gct gta ttt gat gaa ggg				672
Gln Thr Leu His Lys Phe Ile Leu Phe Ala Val Phe Asp Glu Gly				.
210	215	220		.
aaa agt tgg cac tca gaa aca aag aac tcc ttg atg cag gat agg gat				720
Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp				.
225	230	235	240	.
gct gca tct gct cgg gcc tgg cct aaa atg cac aca gtc aat ggt tat				768

Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr			
245	250	255	
gta aac agg tct ctg cca ggt ctg att gga tgc cac agg aaa tca gtc			816
Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val			
260	265	270	
tat tgg cat gtg att gga atg ggc acc act cct gaa gtg cac tca ata			864
Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile			
275	280	285	
ttc ctc gaa ggt cac aca ttt ctt gtg agg aac cat cgc cag gcg tcc			912
Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser			
290	295	300	
ttg gaa atc tcg cca ata act ttc ctt act gctcaa aca ctc ttg atg			960
Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met			
305	310	315	320
gac ctt gga cag ttt cta ctg ttt tgt cat atc tct tcc cac caa cat			1008
Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His			
325	330	335	
gat ggc atg gaa gct tat gtc aaa gta gac agc tgt cca gag gaa ccc			1056
Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro			
340	345	350	
caa cta cga atg aaa aat aat gaa gaa gcg gaa gac tat gat gat gat			1104
Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp			
355	360	365	
ctt act gat tct gaa atg gat gtg gtc agg ttt gat gat gac aac tct			1152
Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser			
370	375	380	
cct tcc ttt atc caa att cgc tca gtt gcc aag aag cat cct aaa act			1200
Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr			
385	390	395	400
tgg gta cat tac att gct gct gaa gag gag gac tgg gac tat gct ccc			1248
Trp Val His Tyr Ile Ala Ala Glu Glu Asp Trp Asp Tyr Ala Pro			
405	410	415	
tta gtc ctc gcc ccc gat gac aga agt tat aaa agt caa tat ttg aac			1296
Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn			
420	425	430	
aat ggc cct cag cgg att ggt agg aag tac aaa aaa gtc cga ttt atg			1344
Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met			
435	440	445	
gca tac aca gat gaa acc ttt aag acg cgt gaa gct att cag cat gaa			1392
Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu			
450	455	460	
tca gga atc ttg gga cct tta ctt tat ggg gaa gtt gga gac aca ctg			1440
Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu			
465	470	475	480
ttg att ata ttt aag aat caa gca agc aga cca tat aac atc tac cct			1488
Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro			
485	490	495	
cac gga atc act gat gtc cgt cct ttg tat tca agg aga tta cca aaa			1536
His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys			
500	505	510	

ggt gta aaa cat ttg aag gat ttt cca att ctg cca gga gaa ata ttc Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe 515 520 525	1584
aaa tat aaa tgg aca gtg act gta gaa gat ggg cca act aaa tca gat Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp 530 535 540	1632
ccg cgg tgc ctg acc cgc tat tac tct agt ttc gtt aat atg gag aga Pro Arg Cys Leu Thr Arg Tyr Ser Ser Phe Val Asn Met Glu Arg 545 550 555 560	1680
gat cta gct tca gga ctc att ggc cct ctc atc tgc tac aaa gaa Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Ile Cys Tyr Lys Glu 565 570 575	1728
tct gta gat caa aga gga aac cag ata atg tca gac aag agg aat gtc Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val 580 585 590	1776
atc ctg ttt tct gta ttt gat gag aac cga agc tgg tac ctc aca gag Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu 595 600 605	1824
aat ata caa cgc ttt ctc ccc aat cca gct gga gtg cag ctt gag gat Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp 610 615 620	1872
cca gag ttc caa gcc tcc aac atc atg cac agc atc aat ggc tat gtt Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val 625 630 635 640	1920
ttt gat agt ttg cag ttg tca gtt tgt ttg cat gag gtg gca tac tgg Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp 645 650 655	1968
tac att cta agc att gga gca cag act gac ttc ctt tct gtc ttc ttc Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe 660 665 670	2016
tct gga tat acc ttc aaa cac aaa atg gtc tat gaa gac aca ctc acc Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr 675 680 685	2064
cta ttc cca ttc tca gga gaa act gtc ttc atg tcg atg gaa aac cca Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro 690 695 700	2112
ggt cta tgg att ctg ggg tgc cac aac tca gac ttt cgg aac aga ggc Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly 705 710 715 720	2160
atg acc gcc tta ctg aag gtt tct agt tgt gac aag aac act ggt gat Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp 725 730 735	2208
tat tac gag gac agt tat gaa gat att tca gca tac ttg ctg agt aaa Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys 740 745 750	2256
aac aat gcc att gaa cct agg agc ttc tct cag aat cca cca gtc ttg Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Pro Pro Val Leu 755 760 765	2304
aaa cgc cat caa cgg gaa ata act cgt act act ctt cag tca gat caa	2352

Lys	Arg	His	Gln	Arg	Glu	Ile	Thr	Arg	Thr	Thr	Leu	Gln	Ser	Asp	Gln		
770						775					780						
gag gaa att gac tat gat gat acc ata tca gtt gaa atg aag aag gaa															2400		
Glu	Glu	Ile	Asp	Tyr	Asp	Asp	Thr	Ile	Ser	Val	Glu	Met	Lys	Lys	Glu		
785						790				795					800		
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Asp	Phe	Asp	Ile	Tyr	Asp	Asp	Glu	Asn	Gln	Ser	Pro	Arg	Ser	Phe			
						805				810				815			
caa aag aaa aca cga cac tat ttt att gct gca gtg gag agg ctc tgg															2496		
Gln	Lys	Lys	Thr	Arg	His	Tyr	Phe	Ile	Ala	Ala	Val	Glu	Arg	Leu	Trp		
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gat tat ggg atg agt agc tcc cca cat gtt cta aga aac agg gct cag															2544		
Asp	Tyr	Gly	Met	Ser	Ser	Pro	His	Val	Leu	Arg	Asn	Arg	Ala	Gln			
						835				840				845			
agt ggc agt gtc cct cag ttc aag aaa gtt gtt ttc cag gaa ttt act															2592		
Ser	Gly	Ser	Val	Pro	Gln	Phe	Lys	Val	Val	Phe	Gln	Glu	Phe	Thr			
						850				855				860			
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Asp	Gly	Ser	Phe	Thr	Gln	Pro	Leu	Tyr	Arg	Gly	Glu	Leu	Asn	Glu	His		
						865				870				875			
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Leu	Gly	Leu	Gly	Pro	Tyr	Ile	Arg	Ala	Glu	Val	Glu	Asp	Asn	Ile			
						885				890				895			
atg gta act ttc aga aat cag gcc tct cgt ccc tat tcc ttc tat tct															2736		
Met	Val	Thr	Phe	Arg	Asn	Gln	Ala	Ser	Arg	Pro	Tyr	Ser	Phe	Tyr	Ser		
						900				905				910			
agc ctt att tct tat gag gaa gat cag agg caa gga gca gaa cct aga															2784		
Ser	Leu	Ile	Ser	Tyr	Glu	Glu	Asp	Gln	Arg	Gln	Gly	Ala	Glu	Pro	Arg		
						915				920				925			
aaa aac ttt gtc aag cct aat gaa acc aaa act tac ttt tgg aaa gtg															2832		
Lys	Asn	Phe	Val	Lys	Pro	Asn	Glu	Thr	Lys	Thr	Tyr	Phe	Trp	Lys	Val		
						930				935				940			
caa cat cat atg gca ccc act aaa gat gag ttt gac tgc aaa gcc tgg															2880		
Gln	His	His	Met	Ala	Pro	Thr	Lys	Asp	Glu	Phe	Asp	Cys	Lys	Ala	Trp		
						945				950				955			
gct tat ttc tct gat gtt gac ctg gaa aaa gat gtg cac tca ggc ctg															2928		
Ala	Tyr	Phe	Ser	Asp	Val	Asp	Leu	Glu	Lys	Asp	Val	His	Ser	Gly	Leu		
						965				970				975			
att gga ccc ctt ctg gtc tgc cac act aac aca ctg aac cct gct cat															2976		
Ile	Gly	Pro	Leu	Leu	Val	Cys	His	Thr	Asn	Thr	Leu	Asn	Pro	Ala	His		
						980				985				990			
ggg aga caa gtg aca gta cag gaa ttt gct ctg ttt ttc acc atc ttt															3024		
Gly	Arg	Gln	Val	Thr	Val	Gln	Glu	Phe	Ala	Leu	Phe	Phe	Thr	Ile	Phe		
						995				1000				1005			
gat gag acc aaa agc tgg tac ttc act gaa aat atg gaa aga aac tgc															3072		
Asp	Glu	Thr	Lys	Ser	Trp	Tyr	Phe	Thr	Glu	Asn	Met	Glu	Arg	Asn	Cys		
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agg gct ccc tgc aat atc cag atg gaa gat ccc act ttt aaa gag aat															3120		
Arg	Ala	Pro	Cys	Asn	Ile	Gln	Met	Glu	Asp	Pro	Thr	Phe	Lys	Glu	Asn		
						1025				1030				1035			
														1040			

tat cgc ttc cat gca atc aat ggc tac ata atg gat aca cta cct ggc Tyr Arg Phe His Ala Ile Asn Gly Tyr Ile Met Asp Thr Leu Pro Gly 1045 1050 1055	3168
tta gta atg gct cag gat caa agg att cga tgg tat ctg ctc agc atg Leu Val Met Ala Gln Asp Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met 1060 1065 1070	3216
ggc agc aat gaa aac atc cat tct att cat ttc agt gga cat gtg ttc Gly Ser Asn Glu Asn Ile His Ser Ile His Phe Ser Gly His Val Phe 1075 1080 1085	3264
act gta cga aaa aaa gag gag tat aaa atg gca ctg tac aat ctc tat Thr Val Arg Lys Lys Glu Glu Tyr Lys Met Ala Leu Tyr Asn Leu Tyr 1090 1095 1100	3312
cca ggt gtt ttt gag aca gtg gaa atg tta cca tcc aaa gct gga att Pro Gly Val Phe Glu Thr Val Glu Met Leu Pro Ser Lys Ala Gly Ile 1105 1110 1115 1120	3360
tgg cgg gtg gaa tgc ctt att ggc gag cat cta cat gct ggg atg agc Trp Arg Val Glu Cys Leu Ile Gly Glu His Leu His Ala Gly Met Ser 1125 1130 1135	3408
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gct tct gga cac att aga gat ttt cag att aca gct tca gga caa tat Ala Ser Gly His Ile Arg Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr 1155 1160 1165	3504
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aag ttc tcc agc ctc tac atc tct cag ttt atc atc atg tat agt ctt Lys Phe Ser Ser Leu Tyr Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu 1220 1225 1230	3696
gat ggg aag aag tgg cag act tat cga gga aat tcc act gga acc tta Asp Gly Lys Lys Trp Gln Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu 1235 1240 1245	3744
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tat agc att cgc agc act ctt cgc atg gag ttg atg ggc tgt gat tta Tyr Ser Ile Arg Ser Thr Leu Arg Met Glu Leu Met Gly Cys Asp Leu 1285 1290 1295	3888
aat agt tgc agc atg cca ttg gga atg gag agt aaa gca ata tca gat	3936

Asn Ser Cys Ser Met Pro Leu Gly Met Glu Ser Lys Ala Ile Ser Asp			
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Ala Gln Ile Thr Ala Ser Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp			
1315	1320	1325	
tct cct tca aaa gct cga ctt cac ctc caa ggg agg agt aat gcc tgg			4032
Ser Pro Ser Lys Ala Arg Leu His Leu Gln Gly Arg Ser Asn Ala Trp			
1330	1335	1340	
aga cct cag gtg aat aat cca aaa gag tgg ctg caa gtg gac ttc cag			4080
Arg Pro Gln Val Asn Asn Pro Lys Glu Trp Leu Gln Val Asp Phe Gln			
1345	1350	1355	1360
aag aca atg aaa gtc aca gga gta act act cag gga gta aaa tct ctg			4128
Lys Thr Met Lys Val Thr Gly Val Thr Gln Gly Val Lys Ser Leu			
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ctt acc agc atg tat gtg aag gag ttc ctc atc tcc agc agt caa gat			4176
Leu Thr Ser Met Tyr Val Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp			
1380	1385	1390	
ggc cat cag tgg act ctc ttt ttt cag aat ggc aaa gta aag gtt ttt			4224
Gly His Gln Trp Thr Leu Phe Gln Asn Gly Lys Val Lys Val Phe			
1395	1400	1405	
cag gga aat caa gac tcc ttc aca cct gtg gtg aac tct cta gac cca			4272
Gln Gly Asn Gln Asp Ser Phe Thr Pro Val Val Asn Ser Leu Asp Pro			
1410	1415	1420	
ccg tta ctg act cgc tac ctt cga att cac ccc cag agt tgg gtg cac			4320
Pro Leu Leu Thr Arg Tyr Leu Arg Ile His Pro Gln Ser Trp Val His			
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cag att gcc ctg agg atg gag gtt ctg ggc tgc gag gca cag gac ctc			4368
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Tyr			

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 35 40 45
 Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val
 50 55 60
 Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Val His Leu Phe Asn Ile
 65 70 75 80
 Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln
 85 90 95
 Ala Glu Val Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser
 100 105 110
 His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser
 115 120 125

Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp
 130 135 140
 Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu
 145 150 155 160
 Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser
 165 170 175
 Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile
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 Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr
 195 200 205
 Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly
 210 215 220
 Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp
 225 230 235 240
 Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr
 245 250 255
 Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val
 260 265 270
 Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile
 275 280 285
 Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser
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 Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met
 305 310 315 320
 Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His
 325 330 335
 Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro
 340 345 350
 Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp
 355 360 365
 Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser
 370 375 380
 Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr
 385 390 395 400
 Trp Val His Tyr Ile Ala Ala Glu Glu Asp Trp Asp Tyr Ala Pro
 405 410 415
 Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn
 420 425 430
 Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met
 435 440 445
 Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu
 450 455 460
 Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu
 465 470 475 480
 Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro
 485 490 495
 His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys
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 Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe
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 Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp
 530 535 540
 Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg
 545 550 555 560
 Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu
 565 570 575
 Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val
 580 585 590
 Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu
 595 600 605
 Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp
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 Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val
 625 630 635 640
 Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp
 645 650 655

Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe
 660 665 670
 Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr
 675 680 685
 Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro
 690 695 700
 Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly
 705 710 715 720
 Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp
 725 730 735
 Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys
 740 745 750
 Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Pro Pro Val Leu
 755 760 765
 Lys Arg His Gln Arg Glu Ile Thr Arg Thr Thr Leu Gln Ser Asp Gln
 770 775 780
 Glu Glu Ile Asp Tyr Asp Asp Thr Ile Ser Val Glu Met Lys Lys Glu
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 Asp Phe Asp Ile Tyr Asp Glu Asp Glu Asn Gln Ser Pro Arg Ser Phe
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 Gln Lys Lys Thr Arg His Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp
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 Asp Tyr Gly Met Ser Ser Pro His Val Leu Arg Asn Arg Ala Gln
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 Ser Gly Ser Val Pro Gln Phe Lys Lys Val Val Phe Gln Glu Phe Thr
 850 855 860
 Asp Gly Ser Phe Thr Gln Pro Leu Tyr Arg Gly Glu Leu Asn Glu His
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 Leu Gly Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile
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 Ser Leu Ile Ser Tyr Glu Glu Asp Gln Arg Gln Gly Ala Glu Pro Arg
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 Lys Asn Phe Val Lys Pro Asn Glu Thr Lys Thr Tyr Phe Trp Lys Val
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 Gln His His Met Ala Pro Thr Lys Asp Glu Phe Asp Cys Lys Ala Trp
 945 950 955 960
 Ala Tyr Phe Ser Asp Val Asp Leu Glu Lys Asp Val His Ser Gly Leu
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 Ile Gly Pro Leu Leu Val Cys His Thr Asn Thr Leu Asn Pro Ala His
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 Gly Arg Gln Val Thr Val Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe
 995 1000 1005
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 Gly Ser Asn Glu Asn Ile His Ser Ile His Phe Ser Gly His Val Phe
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 1090 1095 1100
 Pro Gly Val Phe Glu Thr Val Glu Met Leu Pro Ser Lys Ala Gly Ile
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 Trp Arg Val Glu Cys Leu Ile Gly Glu His Leu His Ala Gly Met Ser
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 Thr Leu Phe Leu Val Tyr Ser Asn Lys Cys Gln Thr Pro Leu Gly Met
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 Ala Ser Gly His Ile Arg Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr
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 Gly Gln Trp Ala Pro Lys Leu Ala Arg Leu His Tyr Ser Gly Ser Ile
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Asn Ala Trp Ser Thr Lys Glu Pro Phe Ser Trp Ile Lys Val Asp Leu
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 Gly Phe Ser Ala Ile Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser
 20 25 30
 tgg gac tac cgg caa agt gaa ctc ctc cgt gag ctg cac gtg gac acc 144
 Trp Asp Tyr Arg Gln Ser Glu Leu Leu Arg Glu Leu His Val Asp Thr
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 Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val

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ctg tac aaa aag act gtg ttc gta gag ttc acg gat caa ctt ttc agc Leu Tyr Lys Lys Thr Val Phe Val Glu Phe Thr Asp Gln Leu Phe Ser 65	70	75	240
gtt gcc agg ccc agg cca cca tgg atg ggt ctg ctg ggt cct acc atc Val Ala Arg Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile 85	90	95	288
cag gct gag gtt tac gac acg gtg gtc gtt acc ctg aag aac atg gct Gln Ala Glu Val Tyr Asp Thr Val Val Val Thr Leu Lys Asn Met Ala 100	105	110	336
tct cat ccc gtt agt ctt cac gct gtc ggc gtc tcc ttc tgg aaa tct Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Phe Trp Lys Ser 115	120	125	384
tcc gaa ggc gct gaa tat gag gat cac acc agc caa agg gag aag gaa Ser Glu Gly Ala Glu Tyr Glu Asp His Thr Ser Gln Arg Glu Lys Glu 130	135	140	432
gac gat aaa gtc ctt ccc ggt aaa agc caa acc tac gtc tgg cag gtc Asp Asp Lys Val Leu Pro Gly Lys Ser Gln Thr Tyr Val Trp Gln Val 145	150	155	480
ctg aaa gaa aat ggt cca aca gcc tct gac cca cca tgt ctt acc tac Leu Lys Glu Asn Gly Pro Thr Ala Ser Asp Pro Pro Cys Leu Thr Tyr 165	170	175	528
tca tac ctg tct cac gtg gac ctg gtg aaa gac ctg aat tcg ggc ctc Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu 180	185	190	576
att gga gcc ctg ctg gtt tgt aga gaa ggg agt ctg acc acc aga gaa agg Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Thr Arg Glu Arg 195	200	205	624
acc cag aac ctg cac gaa ttt gta cta ctt ttt gct gtc ttt gat gaa Thr Gln Asn Leu His Glu Phe Val Leu Leu Phe Ala Val Phe Asp Glu 210	215	220	672
ggg aaa agt tgg cac tca gca aga aat gac tcc tgg aca cgg gcc atg Gly Lys Ser Trp His Ser Ala Arg Asn Asp Ser Trp Thr Arg Ala Met 225	230	235	720
gat ccc gca cct gcc agg gcc cag cct gca atg cac aca gtc aat ggc Asp Pro Ala Pro Ala Arg Ala Gln Pro Ala Met His Thr Val Asn Gly 245	250	255	768
tat gtc aac agg tct ctg cca ggt ctg atc gga tgt cat aag aaa tca Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Lys Lys Ser 260	265	270	816
gtc tac tgg cac gtg att gga atg ggc acc agc ccg gaa gtg cac tcc Val Tyr Trp His Val Ile Gly Met Gly Thr Ser Pro Glu Val His Ser 275	280	285	864
att ttt ctt gaa ggc cac acg ttt ctc gtg agg cac cat cgc cag gct Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg His His Arg Gln Ala 290	295	300	912
tcc ttg gag atc tcg cca cta act ttc ctc act gct cag aca ttc ctg Ser Leu Glu Ile Ser Pro Leu Thr Phe Leu Thr Ala Gln Thr Phe Leu 305	310	315	960

atg gac ctt ggc cag ttc cta ctg ttt tgt cat atc tct tcc cac cac Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His His 325 330 335	1008
cat ggt ggc atg gag gct cac gtc aga gta gaa agc tgc gcc gag gag His Gly Gly Met Glu Ala His Val Arg Val Glu Ser Cys Ala Glu Glu 340 345 350	1056
ccc cag ctg cgg agg aaa gct gat gaa gag gaa gat tat gat gac aat Pro Gln Leu Arg Arg Lys Ala Asp Glu Glu Asp Tyr Asp Asp Asn 355 360 365	1104
ttg tac gac tcg gac atg gac gtg gtc cgg ctc gat ggt gac gac gtg Leu Tyr Asp Ser Asp Met Asp Val Val Arg Leu Asp Gly Asp Asp Val 370 375 380	1152
tct ccc ttt atc caa atc cgc tcg gtt gcc aag aag cat ccc aaa acc Ser Pro Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr 385 390 395 400	1200
tgg gtg cac tac atc tct gca gag gag gac tgg gac tac gcc ccc Trp Val His Tyr Ile Ser Ala Glu Glu Asp Trp Asp Tyr Ala Pro 405 410 415	1248
gcg gtc ccc agc ccc agt gac aga agt tat aaa agt ctc tac ttg aac Ala Val Pro Ser Pro Ser Asp Arg Ser Tyr Lys Ser Leu Tyr Leu Asn 420 425 430	1296
agt ggt cct cag cga att ggt agg aaa tac aaa aaa gct cga ttc gtc Ser Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Ala Arg Phe Val 435 440 445	1344
gct tac acg gat gta aca ttt aag act cgt aaa gct att ccg tat gaa Ala Tyr Thr Asp Val Thr Phe Lys Thr Arg Lys Ala Ile Pro Tyr Glu 450 455 460	1392
tca gga atc ctg gga cct tta ctt tat gga gaa gtt gga gac aca ctt Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Val Glu Asp Thr Leu 465 470 475 480	1440
ttg att ata ttt aag aat aaa gcg agc cga cca tat aac atc tac cct Leu Ile Ile Phe Lys Asn Lys Ala Ser Arg Pro Tyr Asn Ile Tyr Pro 485 490 495	1488
cat gga atc act gat gtc agc gct ttg cac cca ggg aga ctt cta aaa His Gly Ile Thr Asp Val Ser Ala Leu His Pro Gly Arg Leu Leu Lys 500 505 510	1536
ggt tgg aaa cat ttg aaa gac atg cca att ctg cca gga gag act ttc Gly Trp Lys His Leu Lys Asp Met Pro Ile Leu Pro Gly Glu Thr Phe 515 520 525	1584
aag tat aaa tgg aca gtg act gtg gaa gat ggg cca acc aag tcc gat Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp 530 535 540	1632
cct cgg tgc ctg acc cgc tac tac tcg agc tcc att aat cta gag aaa Pro Arg Cys Leu Thr Arg Tyr Ser Ser Ser Ile Asn Leu Glu Lys 545 550 555 560	1680
gat ctg gct tcg gga ctc att ggc cct ctc ctc atc tgc tac aaa gaa Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu 565 570 575	1728
tct gta gac caa aga gga aac cag atg atg tca gac aag aga aac gtc Ser Val Asp Gln Arg Gly Asn Gln Met Met Ser Asp Lys Arg Asn Val	1776

580	585	590	
atc ctg ttt tct gta ttc gat gag aat caa agc tgg tac ctc gca gag Ile Leu Phe Ser Val Phe Asp Glu Asn Gln Ser Trp Tyr Leu Ala Glu 595	600	605	1824
aat att cag cgc ttc ctc ccc aat ccg gat gga tta cag ccc cag gat Asn Ile Gln Arg Phe Leu Pro Asn Pro Asp Gly Leu Gln Pro Gln Asp 610	615	620	1872
cca gag ttc caa gct tct aac atc atg cac agc atc aat ggc tat gtt Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val 625	630	635	1920
ttt gat agc ttg cag ctg tcg gtt tgt ttg cac gag gtg gca tac tgg Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp 645	650	655	1968
tac att cta agt gtt gga gca cag acg gac ttc ctc tcc gtc ttc ttc Tyr Ile Leu Ser Val Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe 660	665	670	2016
tct ggc tac acc ttc aaa cac aaa atg gtc tat gaa gac aca ctc acc Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr 675	680	685	2064
ctg ttc ccc ttc tca gga gaa acg gtc ttc atg tca atg gaa aac cca Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro 690	695	700	2112
ggc ctc tgg gtc ctt ggg tgc cac aac tca gac ttg cgg aac aga ggg Gly Leu Trp Val Leu Gly Cys His Asn Ser Asp Leu Arg Asn Arg Gly 705	710	715	2160
atg aca gcc tta ctg aag gtg tat agt tgt gac agg gac att ggt gat Met Thr Ala Leu Lys Val Tyr Ser Cys Asp Arg Asp Ile Gly Asp 725	730	735	2208
tat tat gac aac act tat gaa gat att cca ggc ttc ttg ctg agt gga Tyr Tyr Asp Asn Thr Tyr Glu Asp Ile Pro Gly Phe Leu Leu Ser Gly 740	745	750	2256
aag aat gtc att gaa cct agg agc ttt gcc cag aat tca aga ccc cct Lys Asn Val Ile Glu Pro Arg Ser Phe Ala Gln Asn Ser Arg Pro Pro 755	760	765	2304
agt gcg agc gct cca aag cct ccg gtc ctg cga cgg cat cag agg gac Ser Ala Ser Ala Pro Lys Pro Val Leu Arg Arg His Gln Arg Asp 770	775	780	2352
ata agc ctt cct act ttt cag ccg gag gaa gac aaa atg gac tat gat Ile Ser Leu Pro Thr Phe Gln Pro Glu Glu Asp Lys Met Asp Tyr Asp 785	790	795	2400
gat atc ttc tca act gaa acg aag gga gaa gat ttt gac att tac ggt Asp Ile Phe Ser Thr Glu Thr Lys Gly Glu Asp Phe Asp Ile Tyr Gly 805	810	815	2448
gag gat gaa aat cag gac cct cgc agc ttt cag aag aga acc cga cac Glu Asp Glu Asn Gln Asp Pro Arg Ser Phe Gln Lys Arg Thr Arg His 820	825	830	2496
tat ttc att gct gcg gtg gag cag ctc tgg gat tac ggg atg agc gaa Tyr Phe Ile Ala Ala Val Glu Gln Leu Trp Asp Tyr Gly Met Ser Glu 835	840	845	2544

tcc ccc cg ^g gc ^g cta aga aac agg gct cag aac gga gag gt ^g cct cg ^g Ser Pro Arg Ala Leu Arg Asn Arg Ala Gln Asn Gly Glu Val Pro Arg 850 855 860	2592
t ^t c aag aag gt ^g gtc t ^t c cg ^g gaa t ^t t gct gac gg ^c tcc t ^t c ac ^g cag Phe Lys Lys Val Val Phe Arg Glu Phe Ala Asp Gly Ser Phe Thr Gln 865 870 875 880	2640
ccg tc ^g tac cg ^c ggg gaa ctc aac aaa cac tt ^g ggg ctc tt ^g gga ccc Pro Ser Tyr Arg Gly Glu Leu Asn Lys His Leu Gly Leu Leu Gly Pro 885 890 895	2688
ta ^c at ^c aga gc ^g gaa gtt gaa gac aac at ^c at ^g gta act t ^t c aaa aac Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val Thr Phe Lys Asn 900 905 910	2736
cag gc ^g tct cgt ccc tat tcc t ^t c tac tc ^g agc ctt att tct tat cc ^g Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Pro 915 920 925	2784
gat gat cag gag caa ggg gca gaa cct cg ^a cac aac t ^t c gtc cag cca Asp Asp Gln Glu Gln Gly Ala Glu Pro Arg His Asn Phe Val Gln Pro 930 935 940	2832
aat gaa acc aga act tac t ^t t tgg aaa gt ^g cag cat cac at ^g gca ccc Asn Glu Thr Arg Thr Tyr Phe Trp Lys Val Gln His His Met Ala Pro 945 950 955 960	2880
aca gaa gac gag t ^t t gac tgc aaa gcc tgg gcc tac t ^t t tct gat gtt Thr Glu Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val 965 970 975	2928
gac ctg gaa aaa gat gt ^g cac tca ggc tt ^g at ^c ggc ccc ctt ctg at ^c Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly Pro Leu Leu Ile 980 985 990	2976
tgc cg ^c gcc aac acc ctg aac gct gct cac ggt aga caa gt ^g acc gt ^g Cys Arg Ala Asn Thr Leu Asn Ala Ala His Gly Arg Gln Val Thr Val 995 1000 1005	3024
caa gaa t ^t t gct ctg t ^t t ttc act att t ^t t gat gag aca aag agc tgg Gln Glu Phe Ala Leu Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp 1010 1015 1020	3072
ta ^c t ^t c act gaa aat gt ^g gaa agg aac tgc cg ^g gcc ccc tgc cat ctg Tyr Phe Thr Glu Asn Val Glu Arg Asn Cys Arg Ala Pro Cys His Leu 1025 1030 1035 1040	3120
cag at ^c gag gac ccc act ctg aaa gaa aac tat cgc t ^t c cat gca at ^c Gln Met Glu Asp Pro Thr Leu Lys Glu Asn Tyr Arg Phe His Ala Ile 1045 1050 1055	3168
aat ggc tat gt ^g at ^c gat aca ctc cct ggc tta gta at ^g gct cag aat Asn Gly Tyr Val Met Asp Thr Leu Pro Gly Leu Val Met Ala Gln Asn 1060 1065 1070	3216
caa agg at ^c cga tgg tat ctg ctc agc at ^c ggc agc aat gaa aat at ^c Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn Ile 1075 1080 1085	3264
cat tc ^g att cat t ^t t agc gga cac gt ^g ttc agt gta cg ^g aaa aag gag His Ser Ile His Phe Ser Gly His Val Phe Ser Val Arg Lys Lys Glu 1090 1095 1100	3312
gag tat aaa at ^c g ^t c gtc tac aat ctc tat cc ^g ggt gtc t ^t t gag aca Glu Tyr Lys Met Ala Val Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr	3360

1105	1110	1115	1120	
gtg gaa atg cta ccg tcc aaa gtt gga att tgg cga ata gaa tgc ctg Val Glu Met Leu Pro Ser Lys Val Gly Ile Trp Arg Ile Glu Cys Leu 1125 1130 1135				3408
att ggc gag cac ctg caa gct ggg atg agc acg act ttc ctg gtg tac Ile Gly Glu His Leu Gln Ala Gly Met Ser Thr Thr Phe Leu Val Tyr 1140 1145 1150				3456
agc aag aag tgt cag act ccc ctg gga atg gct tct gga cac att aga Ser Lys Lys Cys Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile Arg 1155 1160 1165				3504
gat ttt cag att aca gct tca gga caa tat gga cag tgg gcc cca aag Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys 1170 1175 1180				3552
ctg gcc aga ctt cat tat tcc gga tca atc aat gcc tgg agc acc aag Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys 1185 1190 1195 1200				3600
gag ccc ttt tct tgg atc aag gtg gat ctg ttg gca cca atg att att Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile 1205 1210 1215				3648
cac ggc atc aag acc cag ggt gcc cgt cag aag ttc tcc agc ctc tac His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr 1220 1225 1230				3696
atc tct cag ttt atc atc atg tat agt ctt gat ggg aag aag tgg cag Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln 1235 1240 1245				3744
act tat cga gga aat tcc act gga acc tta atg gtc ttc ttt ggc aat Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn 1250 1255 1260				3792
gtg gat tca tct ggg ata aaa cac aat att ttt aac cct cca att att Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Ile 1265 1270 1275 1280				3840
gct cga tac atc cgt ttg cac cca act cat tat agc att cgc agc act Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr 1285 1290 1295				3888
ctt cgc atg gag ttg atg ggc tgt gat tta aat agt tgc agc atg cca Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro 1300 1305 1310				3936
ttg gga atg gag agt aaa gca ata tca gat gca cag att act gct tca Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr Ala Ser 1315 1320 1325				3984
tcc tac ttt acc aat atg ttt gcc acc tgg tct cct tca aaa gct cga Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg 1330 1335 1340				4032
ctt cac ctc caa ggg agg agt aat gcc tgg aga cct cag gtg aat aat Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn Asn 1345 1350 1355 1360				4080
cca aaa gag tgg ctg caa gtg gac ttc cag aag aca atg aaa gtc aca Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val Thr 1365 1370 1375				4128

gga gta act act cag gga gta aaa tct ctg ctt acc agc atg tat gtg Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr Ser Met Tyr Val 1380 1385 1390	4176
aag gag ttc ctc atc tcc agc agt caa gat ggc cat cag tgg act ctc Lys Glu Phe Leu Ile Ser Ser Gln Asp Gly His Gln Trp Thr Leu 1395 1400 1405	4224
ttt ttt cag aat ggc aaa gta aag gtt ttt cag gga aat caa gac tcc Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Gln Asp Ser 1410 1415 1420	4272
ttc aca cct gtg gtg aac tct cta gac cca ccg tta ctg act cgc tac Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr 1425 1430 1435 1440	4320
ctt cga att cac ccc cag agt tgg gtg cac cag att gcc ctg agg atg Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg Met 1445 1450 1455	4368
gag gtt ctg ggc tgc gag gca cag gac ctc tac Glu Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr 1460 1465	4401

<210> 15
 <211> 1467
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> HP44/OL-- factor VIII having the following
 domains: A1p-A2p-app-A3p-C1h-C2h

<400> 15
 Met Gln Leu Glu Leu Ser Thr Cys Val Phe Leu Cys Leu Leu Pro Leu
 1 5 10 15
 Gly Phe Ser Ala Ile Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser
 20 25 30
 Trp Asp Tyr Arg Gln Ser Glu Leu Leu Arg Glu Leu His Val Asp Thr
 35 40 45
 Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val
 50 55 60
 Leu Tyr Lys Lys Thr Val Phe Val Glu Phe Thr Asp Gln Leu Phe Ser
 65 70 75 80
 Val Ala Arg Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile
 85 90 95
 Gln Ala Glu Val Tyr Asp Thr Val Val Val Thr Leu Lys Asn Met Ala
 100 105 110
 Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Phe Trp Lys Ser
 115 120 125
 Ser Glu Gly Ala Glu Tyr Glu Asp His Thr Ser Gln Arg Glu Lys Glu
 130 135 140
 Asp Asp Lys Val Leu Pro Gly Lys Ser Gln Thr Tyr Val Trp Gln Val
 145 150 155 160
 Leu Lys Glu Asn Gly Pro Thr Ala Ser Asp Pro Pro Cys Leu Thr Tyr
 165 170 175
 Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu
 180 185 190
 Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Thr Arg Glu Arg
 195 200 205
 Thr Gln Asn Leu His Glu Phe Val Leu Leu Phe Ala Val Phe Asp Glu
 210 215 220
 Gly Lys Ser Trp His Ser Ala Arg Asn Asp Ser Trp Thr Arg Ala Met
 225 230 235 240
 Asp Pro Ala Pro Ala Arg Ala Gln Pro Ala Met His Thr Val Asn Gly

245	250	255
Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Lys Lys Ser		
260	265	270
Val Tyr Trp His Val Ile Gly Met Gly Thr Ser Pro Glu Val His Ser		
275	280	285
Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg His His Arg Gln Ala		
290	295	300
Ser Leu Glu Ile Ser Pro Leu Thr Phe Leu Thr Ala Gln Thr Phe Leu		
305	310	315
Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His His		
325	330	335
His Gly Gly Met Glu Ala His Val Arg Val Glu Ser Cys Ala Glu Glu		
340	345	350
Pro Gln Leu Arg Arg Lys Ala Asp Glu Glu Glu Asp Tyr Asp Asp Asn		
355	360	365
Leu Tyr Asp Ser Asp Met Asp Val Val Arg Leu Asp Gly Asp Asp Val		
370	375	380
Ser Pro Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr		
385	390	395
Trp Val His Tyr Ile Ser Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro		
405	410	415
Ala Val Pro Ser Pro Ser Asp Arg Ser Tyr Lys Ser Leu Tyr Leu Asn		
420	425	430
Ser Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Ala Arg Phe Val		
435	440	445
Ala Tyr Thr Asp Val Thr Phe Lys Thr Arg Lys Ala Ile Pro Tyr Glu		
450	455	460
Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu		
465	470	475
Leu Ile Ile Phe Lys Asn Lys Ala Ser Arg Pro Tyr Asn Ile Tyr Pro		
485	490	495
His Gly Ile Thr Asp Val Ser Ala Leu His Pro Gly Arg Leu Leu Lys		
500	505	510
Gly Trp Lys His Leu Lys Asp Met Pro Ile Leu Pro Gly Glu Thr Phe		
515	520	525
Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp		
530	535	540
Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Ile Asn Leu Glu Lys		
545	550	555
Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu		
565	570	575
Ser Val Asp Gln Arg Gly Asn Gln Met Met Ser Asp Lys Arg Asn Val		
580	585	590
Ile Leu Phe Ser Val Phe Asp Glu Asn Gln Ser Trp Tyr Leu Ala Glu		
595	600	605
Asn Ile Gln Arg Phe Leu Pro Asn Pro Asp Gly Leu Gln Pro Gln Asp		
610	615	620
Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val		
625	630	635
Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp		
645	650	655
Tyr Ile Leu Ser Val Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe		
660	665	670
Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr		
675	680	685
Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro		
690	695	700
Gly Leu Trp Val Leu Gly Cys His Asn Ser Asp Leu Arg Asn Arg Gly		
705	710	715
Met Thr Ala Leu Leu Lys Val Tyr Ser Cys Asp Arg Asp Ile Gly Asp		
725	730	735
Tyr Tyr Asp Asn Thr Tyr Glu Asp Ile Pro Gly Phe Leu Leu Ser Gly		
740	745	750
Lys Asn Val Ile Glu Pro Arg Ser Phe Ala Gln Asn Ser Arg Pro Pro		
755	760	765
Ser Ala Ser Ala Pro Lys Pro Pro Val Leu Arg Arg His Gln Arg Asp		

770	775	780
Ile Ser Leu Pro Thr Phe Gln Pro Glu Glu Asp Lys Met Asp Tyr Asp		
785	790	795
Asp Ile Phe Ser Thr Glu Thr Lys Gly Glu Asp Phe Asp Ile Tyr Gly		800
805	810	815
Glu Asp Glu Asn Gln Asp Pro Arg Ser Phe Gln Lys Arg Thr Arg His		
820	825	830
Tyr Phe Ile Ala Ala Val Glu Gln Leu Trp Asp Tyr Gly Met Ser Glu		
835	840	845
Ser Pro Arg Ala Leu Arg Asn Arg Ala Gln Asn Gly Glu Val Pro Arg		
850	855	860
Phe Lys Lys Val Val Phe Arg Glu Phe Ala Asp Gly Ser Phe Thr Gln		
865	870	875
880		
Pro Ser Tyr Arg Gly Glu Leu Asn Lys His Leu Gly Leu Leu Gly Pro		
885	890	895
Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val Thr Phe Lys Asn		
900	905	910
Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Pro		
915	920	925
Asp Asp Gln Glu Gln Gly Ala Glu Pro Arg His Asn Phe Val Gln Pro		
930	935	940
Asn Glu Thr Arg Thr Tyr Phe Trp Lys Val Gln His His Met Ala Pro		
945	950	955
960		
Thr Glu Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val		
965	970	975
Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly Pro Leu Leu Ile		
980	985	990
Cys Arg Ala Asn Thr Leu Asn Ala Ala His Gly Arg Gln Val Thr Val		
995	1000	1005
Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp		
1010	1015	1020
Tyr Phe Thr Glu Asn Val Glu Arg Asn Cys Arg Ala Pro Cys His Leu		
1025	1030	1035
1040		
Gln Met Glu Asp Pro Thr Leu Lys Glu Asn Tyr Arg Phe His Ala Ile		
1045	1050	1055
Asn Gly Tyr Val Met Asp Thr Leu Pro Gly Leu Val Met Ala Gln Asn		
1060	1065	1070
Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn Ile		
1075	1080	1085
His Ser Ile His Phe Ser Gly His Val Phe Ser Val Arg Lys Lys Glu		
1090	1095	1100
Glu Tyr Lys Met Ala Val Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr		
1105	1110	1115
1120		
Val Glu Met Leu Pro Ser Lys Val Gly Ile Trp Arg Ile Glu Cys Leu		
1125	1130	1135
Ile Gly Glu His Leu Gln Ala Gly Met Ser Thr Thr Phe Leu Val Tyr		
1140	1145	1150
Ser Lys Lys Cys Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile Arg		
1155	1160	1165
Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys		
1170	1175	1180
Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys		
1185	1190	1195
1200		
Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile		
1205	1210	1215
His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr		
1220	1225	1230
Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln		
1235	1240	1245
Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn		
1250	1255	1260
Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Ile		
1265	1270	1275
1280		
Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr		
1285	1290	1295
Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro		

1300	1305	1310													
Leu	Gly	Met	Glu	Ser	Lys	Ala	Ile	Ser	Asp	Ala	Gln	Ile	Thr	Ala	Ser
1315															1325
Ser	Tyr	Phe	Thr	Asn	Met	Phe	Ala	Thr	Trp	Ser	Pro	Ser	Lys	Ala	Arg
1330															1340
Leu	His	Leu	Gln	Gly	Arg	Ser	Asn	Ala	Trp	Arg	Pro	Gln	Val	Asn	Asn
1345															1360
Pro	Lys	Glu	Trp	Leu	Gln	Val	Asp	Phe	Gln	Lys	Thr	Met	Lys	Val	Thr
1365															1375
Gly	Val	Thr	Gln	Gly	Val	Lys	Ser	Leu	Leu	Thr	Ser	Met	Tyr	Val	
1380															1390
Lys	Glu	Phe	Leu	Ile	Ser	Ser	Ser	Gln	Asp	Gly	His	Gln	Trp	Thr	Leu
1395															1405
Phe	Phe	Gln	Asn	Gly	Lys	Val	Lys	Val	Phe	Gln	Gly	Asn	Gln	Asp	Ser
1410															1420
Phe	Thr	Pro	Val	Val	Asn	Ser	Leu	Asp	Pro	Pro	Leu	Leu	Thr	Arg	Tyr
1425															1440
Leu	Arg	Ile	His	Pro	Gln	Ser	Trp	Val	His	Gln	Ile	Ala	Leu	Arg	Met
1445															1455
Glu	Val	Leu	Gly	Cys	Glu	Ala	Gln	Asp	Leu	Tyr					
1460															1465

<210> 16

<211> 4371

<212> DNA

<213> Artificial Sequence

<220>

<223> hybrid human and porcine factor VIII sequence

<221> CDS

<222> (1)...(4371)

<223> HP46/SQ-- factor VIII having the following domains: A1p-A2h-aph-A3h-C1h-C2h

<400> 16

atg	cag	cta	gag	ctc	tcc	acc	tgt	gtc	ttt	ctg	tgt	ctc	ttg	cca	ctc
Met	Gln	Leu	Glu	Leu	Ser	Thr	Cys	Val	Phe	Leu	Cys	Leu	Leu	Pro	Leu
1															15

48

ggc	ttt	agt	gcc	atc	agg	aga	tac	tac	ctg	ggc	gca	gtg	gaa	ctg	tcc
Gly	Phe	Ser	Ala	Ile	Arg	Arg	Tyr	Tyr	Leu	Gly	Ala	Val	Glu	Leu	Ser
20															30

96

tgg	gac	tac	cg	caa	agt	gaa	ctc	ctc	cgt	gag	ctg	cac	gtg	gac	acc
Trp	Asp	Tyr	Arg	Gln	Ser	Glu	Leu	Leu	Arg	Glu	Leu	His	Val	Asp	Thr
35															45

144

aga	ttt	cct	gct	aca	g	cg	cca	g	ga	ct	cc	tg	cc	tca	gtc	
Arg	Phe	Pro	Ala	Thr	A	l	Pro	G	Ala	Leu	Pro	Leu	Gly	Pro	Ser	Val
50															60	

192

ctg	tac	aaa	aag	act	gt	t	tc	gt	gag	tt	ac	gt	caa	ctt	ttc	agc
Leu	Tyr	Lys	Lys	Thr	Val	Phe	Val	Glu	Phe	Thr	Asp	Gln	Leu	Phe	Ser	
65															80	

240

gtt	gcc	agg	ccc	agg	cc	cca	tgg	atg	gg	ctg	ctg	gg	cct	acc	atc
Val	Ala	Arg	Pro	Arg	Pro	Pro	Trp	Met	Gly	Leu	Leu	Gly	Pro	Thr	Ile
85															95

288

cag	gct	gag	gtt	tac	gac	acg	gt	gt	gtt	acc	ctg	aag	aac	atg	gct
Gln	Ala	Glu	Val	Tyr	Asp	Thr	Val	Val	Val	Thr	Leu	Lys	Asn	Met	Ala
100															110

336

tct	cat	ccc	gtt	agt	ctt	cac	gct	gt	gc	gt	tcc	ttc	tgg	aaa	tct
-----	-----	-----	-----	-----	-----	-----	-----	----	----	----	-----	-----	-----	-----	-----

384

Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Phe Trp Lys Ser			
115	120	125	
tcc gaa ggc gct gaa tat gag gat cac acc agc caa agg gag aag gaa			432
Ser Glu Gly Ala Glu Tyr Glu Asp His Thr Ser Gln Arg Glu Lys Glu			
130	135	140	
gac gat aaa gtc ctt ccc ggt aaa agc caa acc tac gtc tgg cag gtc			480
Asp Asp Lys Val Leu Pro Gly Lys Ser Gln Thr Tyr Val Trp Gln Val			
145	150	155	160
ctg aaa gaa aat ggt cca aca gcc tct gac cca cca tgt ctt acc tac			528
Leu Lys Glu Asn Gly Pro Thr Ala Ser Asp Pro Pro Cys Leu Thr Tyr			
165	170	175	
tca tac ctg tct cac gtg gac ctg gtg aaa gac ctg aat tcg ggc ctc			576
Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu			
180	185	190	
att gga gcc ctg ctg gtt tgt aga gaa ggg agt ctg acc aga gaa agg			624
Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Thr Arg Glu Arg			
195	200	205	
acc cag aac ctg cac gaa ttt gta cta ctt ttt gct gtc ttt gat gaa			672
Thr Gln Asn Leu His Glu Phe Val Leu Leu Phe Ala Val Phe Asp Glu			
210	215	220	
ggg aaa agt tgg cac tca gca aga aat gac tcc tgg aca cgg gcc atg			720
Gly Lys Ser Trp His Ser Ala Arg Asn Asp Ser Trp Thr Arg Ala Met			
225	230	235	240
gat ccc gca cct gcc agg gcc cag cct gca atg cac aca gtc aat ggc			768
Asp Pro Ala Pro Ala Arg Ala Gln Pro Ala Met His Thr Val Asn Gly			
245	250	255	
tat gtc aac agg tct ctg cca ggt ctg atc gga tgt cat aag aaa tca			816
Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Lys Lys Ser			
260	265	270	
gtc tac tgg cac gtg att gga atg ggc acc agc ccg gaa gtg cac tcc			864
Val Tyr Trp His Val Ile Gly Met Gly Thr Ser Pro Glu Val His Ser			
275	280	285	
att ttt ctt gaa ggc cac acg ttt ctc gtg agg cac cat cgc cag gct			912
Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg His His Arg Gln Ala			
290	295	300	
tcc ttg gag atc tcg cca cta act ttc ctc act gct cag aca ttc ctg			960
Ser Leu Glu Ile Ser Pro Leu Thr Phe Leu Thr Ala Gln Thr Phe Leu			
305	310	315	320
atg gac ctt ggc cag ttc cta ctg ttt tgt cat atc tct tcc cac cac			1008
Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His His			
325	330	335	
cat ggt ggc atg gag gct cac gtc aga gta gaa agc tgc gcc gag gag			1056
His Gly Gly Met Glu Ala His Val Arg Val Glu Ser Cys Ala Glu Glu			
340	345	350	
ccc cag ctg cgg agg aaa gct gat gaa gag gaa gat tat gat gac aat			1104
Pro Gln Leu Arg Arg Lys Ala Asp Glu Glu Asp Tyr Asp Asp Asn			
355	360	365	
ttg tac gac tcg gac atg gac gtg gtc cgg ctc gat ggt gac gac gtg			1152
Leu Tyr Asp Ser Asp Met Asp Val Val Arg Leu Asp Gly Asp Asp Val			
370	375	380	

tct ccc ttt atc caa atc cgc tca gtt gcc aag aag cat cct aaa act Ser Pro Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr 385 390 395 400	1200
tgg gta cat tac att gct gct gaa gag gag gac tgg gac tat gct ccc Trp Val His Tyr Ile Ala Ala Glu Glu Asp Trp Asp Tyr Ala Pro 405 410 415	1248
tta gtc ctc gcc ccc gat gac aga agt tat aaa agt caa tat ttg aac Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn 420 425 430	1296
aat ggc cct cag cgg att ggt agg aag tac aaa aaa gtc cga ttt atg Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met 435 440 445	1344
gca tac aca gat gaa acc ttt aag acg cgt gaa gct att cag cat gaa Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu 450 455 460	1392
tca gga atc ttg gga cct tta ctt tat ggg gaa gtt gga gac aca ctg Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu 465 470 475 480	1440
ttg att ata ttt aag aat caa gca agc aga cca tat aac atc tac cct Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro 485 490 495	1488
cac gga atc act gat gtc cgt cct ttg tat tca agg aga tta cca aaa His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys 500 505 510	1536
ggg gta aaa cat ttg aag gat ttt cca att ctg cca gga gaa ata ttc Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe 515 520 525	1584
aaa tat aaa tgg aca gtg act gta gaa gat ggg cca act aaa tca gat Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp 530 535 540	1632
ccg cgg tgc ctg acc cgc tat tac tct agt ttc gtt aat atg gag aga Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg 545 550 555 560	1680
gat cta gct tca gga ctc att ggc cct ctc atc tgc tac aaa gaa Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu 565 570 575	1728
tct gta gat caa aga gga aac cag ata atg tca gac aag agg aat gtc Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val 580 585 590	1776
atc ctg ttt tct gta ttt gat gag aac cga agc tgg tac ctc aca gag Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu 595 600 605	1824
aat ata caa cgc ttt ctc ccc aat cca gct gga gtg cag ctt gag gat Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp 610 615 620	1872
cca gag ttc caa gcc tcc aac atc atg cac agc atc aat ggc tat gtt Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val 625 630 635 640	1920
ttt gat agt ttg cag ttg tca gtt tgt ttg cat gag gtg gca tac tgg	1968

Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp			
645	650	655	
tac att cta agc att gga gca cag act gac ttc ctt tct gtc ttc ttc			2016
Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe			
660	665	670	
tct gga tat acc ttc aaa cac aaa atg gtc tat gaa gac aca ctc acc			2064
Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr			
675	680	685	
cta ttc cca ttc tca gga gaa act gtc ttc atg tcg atg gaa aac cca			2112
Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro			
690	695	700	
ggc cta tgg att ctg ggg tgc cac aac tca gac ttt cgg aac aga ggc			2160
Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly			
705	710	715	720
atg acc gcc tta ctg aag gtt tct agt tgt gac aag aac act ggt gat			2208
Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp			
725	730	735	
tat tac gag gac agt tat gaa gat att tca gca tac ttg ctg agt aaa			2256
Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys			
740	745	750	
aac aat gcc att gaa cct agg agc ttc tct cag aat cca cca gtc ttg			2304
Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Pro Pro Val Leu			
755	760	765	
aaa cgc cat caa cgg gaa ata act cgt act act ctt cag tca gat caa			2352
Lys Arg His Gln Arg Glu Ile Thr Arg Thr Thr Leu Gln Ser Asp Gln			
770	775	780	
gag gaa att gac tat gat gat acc ata tca gtt gaa atg aag aag gaa			2400
Glu Glu Ile Asp Tyr Asp Asp Thr Ile Ser Val Glu Met Lys Lys Glu			
785	790	795	800
gat ttt gac att tat gat gag gat gaa aat cag agc ccc cgc agc ttt			2448
Asp Phe Asp Ile Tyr Asp Glu Asp Glu Asn Gln Ser Pro Arg Ser Phe			
805	810	815	
caa aag aaa aca cga cac tat ttt att gct gca gtg gag agg ctc tgg			2496
Gln Lys Lys Thr Arg His Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp			
820	825	830	
gat tat ggg atg agt agc tcc cca cat gtt cta aga aac agg gct cag			2544
Asp Tyr Gly Met Ser Ser Ser Pro His Val Leu Arg Asn Arg Ala Gln			
835	840	845	
agt ggc agt gtc cct cag ttc aag aaa gtt gtt ttc cag gaa ttt act			2592
Ser Gly Ser Val Pro Gln Phe Lys Lys Val Val Phe Gln Glu Phe Thr			
850	855	860	
gat ggc tcc ttt act cag ccc tta tac cgt gga gaa cta aat gaa cat			2640
Asp Gly Ser Phe Thr Gln Pro Leu Tyr Arg Gly Glu Leu Asn Glu His			
865	870	875	880
ttg gga ctc ctg ggg cca tat ata aga gca gaa gtt gaa gat aat atc			2688
Leu Gly Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile			
885	890	895	
atg gta act ttc aga aat cag gcc tct cgt ccc tat tcc ttc tat tct			2736
Met Val Thr Phe Arg Asn Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser			
900	905	910	

agc ctt att tct tat gag gaa gat cag agg caa gga gca gaa cct aga Ser Leu Ile Ser Tyr Glu Glu Asp Gln Arg Gln Gly Ala Glu Pro Arg 915 920 925	2784
aaa aac ttt gtc aag cct aat gaa acc aaa act tac ttt tgg aaa gtg Lys Asn Phe Val Lys Pro Asn Glu Thr Lys Thr Tyr Phe Trp Lys Val 930 935 940	2832
caa cat cat atg gca ccc act aaa gat gag ttt gac tgc aaa gcc tgg Gln His His Met Ala Pro Thr Lys Asp Glu Phe Asp Cys Lys Ala Trp 945 950 955 960	2880
gct tat ttc tct gat gtt gac ctg gaa aaa gat gtg cac tca ggc ctg Ala Tyr Phe Ser Asp Val Asp Leu Glu Lys Asp Val His Ser Gly Leu 965 970 975	2928
att gga ccc ctt ctg gtc tgc cac act aac aca ctg aac cct gct cat Ile Gly Pro Leu Leu Val Cys His Thr Asn Thr Leu Asn Pro Ala His 980 985 990	2976
ggg aga caa gtg aca gta cag gaa ttt gct ctg ttt ttc acc atc ttt Gly Arg Gln Val Thr Val Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe 995 1000 1005	3024
gat gag acc aaa agc tgg tac ttc act gaa aat atg gaa aga aac tgc Asp Glu Thr Lys Ser Trp Tyr Phe Thr Glu Asn Met Glu Arg Asn Cys 1010 1015 1020	3072
agg gct ccc tgc aat atc cag atg gaa gat ccc act ttt aaa gag aat Arg Ala Pro Cys Asn Ile Gln Met Glu Asp Pro Thr Phe Lys Glu Asn 1025 1030 1035 1040	3120
tat cgc ttc cat gca atc aat ggc tac ata atg gat aca cta cct ggc Tyr Arg Phe His Ala Ile Asn Gly Tyr Ile Met Asp Thr Leu Pro Gly 1045 1050 1055	3168
tta gta atg gct cag gat caa agg att cga tgg tat ctg ctc agc atg Leu Val Met Ala Gln Asp Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met 1060 1065 1070	3216
ggc agc aat gaa aac atc cat tct att cat ttc agt gga cat gtg ttc Gly Ser Asn Glu Asn Ile His Ser Ile His Phe Ser Gly His Val Phe 1075 1080 1085	3264
act gta cga aaa aaa gag gag tat aaa atg gca ctg tac aat ctc tat Thr Val Arg Lys Lys Glu Glu Tyr Lys Met Ala Leu Tyr Asn Leu Tyr 1090 1095 1100	3312
cca ggt gtt ttt gag aca gtg gaa atg tta cca tcc aaa gct gga att Pro Gly Val Phe Glu Thr Val Glu Met Leu Pro Ser Lys Ala Gly Ile 1105 1110 1115 1120	3360
tgg cgg gtg gaa tgc ctt att ggc gag cat cta cat gct ggg atg agc Trp Arg Val Glu Cys Leu Ile Gly Glu His Leu His Ala Gly Met Ser 1125 1130 1135	3408
aca ctt ttt ctg gtg tac agc aat aag tgt cag act ccc ctg gga atg Thr Leu Phe Leu Val Tyr Ser Asn Lys Cys Gln Thr Pro Leu Gly Met 1140 1145 1150	3456
gct tct gga cac att aga gat ttt cag att aca gct tca gga caa tat Ala Ser Gly His Ile Arg Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr 1155 1160 1165	3504
gga cag tgg gcc cca aag ctg gcc aga ctt cat tat tcc gga tca atc	3552

Gly Gln Trp Ala Pro Lys Leu Ala Arg Leu His Tyr Ser Gly Ser Ile		
1170	1175	1180
aat gcc tgg agc acc aag gag ccc ttt tct tgg atc aag gtg gat ctg	3600	
Asn Ala Trp Ser Thr Lys Glu Pro Phe Ser Trp Ile Lys Val Asp Leu		
1185	1190	1195
1200		
ttg gca cca atg att att cac ggc atc aag acc cag ggt gcc cgt cag	3648	
Leu Ala Pro Met Ile Ile His Gly Ile Lys Thr Gln Gly Ala Arg Gln		
1205	1210	1215
aag ttc tcc agc ctc tac atc tct cag ttt atc atc atg tat agt ctt	3696	
Lys Phe Ser Ser Leu Tyr Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu		
1220	1225	1230
gat ggg aag aag tgg cag act tat cga gga aat tcc act gga acc tta	3744	
Asp Gly Lys Lys Trp Gln Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu		
1235	1240	1245
atg gtc ttc ttt ggc aat gtc gat tca tct ggg ata aaa cac aat att	3792	
Met Val Phe Phe Gly Asn Val Asp Ser Ser Gly Ile Lys His Asn Ile		
1250	1255	1260
ttt aac cct cca att att gct cga tac atc cgt ttg cac cca act cat	3840	
Phe Asn Pro Pro Ile Ile Ala Arg Tyr Ile Arg Leu His Pro Thr His		
1265	1270	1275
1280		
tat agc att cgc agc act ctt cgc atg gag ttg atg ggc tgt gat tta	3888	
Tyr Ser Ile Arg Ser Thr Leu Arg Met Glu Leu Met Gly Cys Asp Leu		
1285	1290	1295
aat agt tgc agc atg cca ttg gga atg gag agt aaa gca ata tca gat	3936	
Asn Ser Cys Ser Met Pro Leu Gly Met Glu Ser Lys Ala Ile Ser Asp		
1300	1305	1310
gca cag att act gct tca tcc tac ttt acc aat atg ttt gcc acc tgg	3984	
Ala Gln Ile Thr Ala Ser Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp		
1315	1320	1325
tct cct tca aaa gct cga ctt cac ctc caa ggg agg agt aat gcc tgg	4032	
Ser Pro Ser Lys Ala Arg Leu His Leu Gln Gly Arg Ser Asn Ala Trp		
1330	1335	1340
aga cct cag gtg aat aat cca aaa gag tgg ctg caa gtg gac ttc cag	4080	
Arg Pro Gln Val Asn Asn Pro Lys Glu Trp Leu Gln Val Asp Phe Gln		
1345	1350	1355
1360		
aag aca atg aaa gtc aca gga gta act act cag gga gta aaa tct ctg	4128	
Lys Thr Met Lys Val Thr Gly Val Thr Gln Gly Val Lys Ser Leu		
1365	1370	1375
ctt acc agc atg tat gtg aag gag ttc ctc atc tcc agc agt caa gat	4176	
Leu Thr Ser Met Tyr Val Lys Glu Phe Leu Ile Ser Ser Gln Asp		
1380	1385	1390
ggc cat cag tgg act ctc ttt ttt cag aat ggc aaa gta aag gtt ttt	4224	
Gly His Gln Trp Thr Leu Phe Phe Gln Asn Gly Lys Val Lys Val Phe		
1395	1400	1405
cag gga aat caa gac tcc ttc aca cct gtg gtg aac tct cta gac cca	4272	
Gln Gly Asn Gln Asp Ser Phe Thr Pro Val Val Asn Ser Leu Asp Pro		
1410	1415	1420
ccg tta ctg act cgc tac ctt cga att cac ccc cag agt tgg gtg cac	4320	
Pro Leu Leu Thr Arg Tyr Leu Arg Ile His Pro Gln Ser Trp Val His		
1425	1430	1435
1440		

cag att gcc ctg agg atg gag gtt ctg ggc tgc gag gca cag gac ctc 4368
Gln Ile Ala Leu Arg Met Glu Val Leu Gly Cys Glu Ala Gln Asp Leu
1445 1450 1455

tac 4371
Tyr

<210> 17
<211> 1457
<212> PRT
<213> Artificial Sequence

<220>
<223> HP46/SQ-- factor VIII having the following
domains: A1p-A2h-aph-A3h-C1h-C2h

<400> 17
Met Gln Leu Glu Leu Ser Thr Cys Val Phe Leu Cys Leu Leu Pro Leu
1 5 10 15
Gly Phe Ser Ala Ile Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser
20 25 30
Trp Asp Tyr Arg Gln Ser Glu Leu Leu Arg Glu Leu His Val Asp Thr
35 40 45
Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val
50 55 60
Leu Tyr Lys Lys Thr Val Phe Val Glu Phe Thr Asp Gln Leu Phe Ser
65 70 75 80
Val Ala Arg Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile
85 90 95
Gln Ala Glu Val Tyr Asp Thr Val Val Val Thr Leu Lys Asn Met Ala
100 105 110
Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Phe Trp Lys Ser
115 120 125
Ser Glu Gly Ala Glu Tyr Glu Asp His Thr Ser Gln Arg Glu Lys Glu
130 135 140
Asp Asp Lys Val Leu Pro Gly Lys Ser Gln Thr Tyr Val Trp Gln Val
145 150 155 160
Leu Lys Glu Asn Gly Pro Thr Ala Ser Asp Pro Pro Cys Leu Thr Tyr
165 170 175
Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu
180 185 190
Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Thr Arg Glu Arg
195 200 205
Thr Gln Asn Leu His Glu Phe Val Leu Leu Phe Ala Val Phe Asp Glu
210 215 220
Gly Lys Ser Trp His Ser Ala Arg Asn Asp Ser Trp Thr Arg Ala Met
225 230 235 240
Asp Pro Ala Pro Ala Arg Ala Gln Pro Ala Met His Thr Val Asn Gly
245 250 255
Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Lys Lys Ser
260 265 270
Val Tyr Trp His Val Ile Gly Met Gly Thr Ser Pro Glu Val His Ser
275 280 285
Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg His His Arg Gln Ala
290 295 300
Ser Leu Glu Ile Ser Pro Leu Thr Phe Leu Thr Ala Gln Thr Phe Leu
305 310 315 320
Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His His
325 330 335
His Gly Gly Met Glu Ala His Val Arg Val Glu Ser Cys Ala Glu Glu
340 345 350
Pro Gln Leu Arg Arg Lys Ala Asp Glu Glu Asp Tyr Asp Asp Asn
355 360 365

Leu Tyr Asp Ser Asp Met Asp Val Val Arg Leu Asp Gly Asp Asp Val
 370 375 380
 Ser Pro Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr
 385 390 395 400
 Trp Val His Tyr Ile Ala Ala Glu Glu Asp Trp Asp Tyr Ala Pro
 405 410 415
 Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn
 420 425 430
 Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met
 435 440 445
 Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu
 450 455 460
 Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu
 465 470 475 480
 Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro
 485 490 495
 His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys
 500 505 510
 Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe
 515 520 525
 Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp
 530 535 540
 Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg
 545 550 555 560
 Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu
 565 570 575
 Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val
 580 585 590
 Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu
 595 600 605
 Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp
 610 615 620
 Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val
 625 630 635 640
 Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp
 645 650 655
 Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe
 660 665 670
 Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr
 675 680 685
 Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro
 690 695 700
 Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly
 705 710 715 720
 Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp
 725 730 735
 Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys
 740 745 750
 Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Pro Pro Val Leu
 755 760 765
 Lys Arg His Gln Arg Glu Ile Thr Arg Thr Thr Leu Gln Ser Asp Gln
 770 775 780
 Glu Glu Ile Asp Tyr Asp Asp Thr Ile Ser Val Glu Met Lys Lys Glu
 785 790 795 800
 Asp Phe Asp Ile Tyr Asp Glu Asp Glu Asn Gln Ser Pro Arg Ser Phe
 805 810 815
 Gln Lys Lys Thr Arg His Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp
 820 825 830
 Asp Tyr Gly Met Ser Ser Ser Pro His Val Leu Arg Asn Arg Ala Gln
 835 840 845
 Ser Gly Ser Val Pro Gln Phe Lys Lys Val Val Phe Gln Glu Phe Thr
 850 855 860
 Asp Gly Ser Phe Thr Gln Pro Leu Tyr Arg Gly Glu Leu Asn Glu His
 865 870 875 880
 Leu Gly Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile
 885 890 895

Met Val Thr Phe Arg Asn Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser .
 900 905 910
 Ser Leu Ile Ser Tyr Glu Glu Asp Gln Arg Gln Gly Ala Glu Pro Arg
 915 920 925
 Lys Asn Phe Val Lys Pro Asn Glu Thr Lys Thr Tyr Phe Trp Lys Val
 930 935 940
 Gln His His Met Ala Pro Thr Lys Asp Glu Phe Asp Cys Lys Ala Trp
 945 950 955 960
 Ala Tyr Phe Ser Asp Val Asp Leu Glu Lys Asp Val His Ser Gly Leu
 965 970 975
 Ile Gly Pro Leu Leu Val Cys His Thr Asn Thr Leu Asn Pro Ala His
 980 985 990
 Gly Arg Gln Val Thr Val Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe
 995 1000 1005
 Asp Glu Thr Lys Ser Trp Tyr Phe Thr Glu Asn Met Glu Arg Asn Cys
 1010 1015 1020
 Arg Ala Pro Cys Asn Ile Gln Met Glu Asp Pro Thr Phe Lys Glu Asn
 1025 1030 1035 1040
 Tyr Arg Phe His Ala Ile Asn Gly Tyr Ile Met Asp Thr Leu Pro Gly
 1045 1050 1055
 Leu Val Met Ala Gln Asp Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met
 1060 1065 1070
 Gly Ser Asn Glu Asn Ile His Ser Ile His Phe Ser Gly His Val Phe
 1075 1080 1085
 Thr Val Arg Lys Lys Glu Glu Tyr Lys Met Ala Leu Tyr Asn Leu Tyr
 1090 1095 1100
 Pro Gly Val Phe Glu Thr Val Glu Met Leu Pro Ser Lys Ala Gly Ile
 1105 1110 1115 1120
 Trp Arg Val Glu Cys Leu Ile Gly Glu His Leu His Ala Gly Met Ser
 1125 1130 1135
 Thr Leu Phe Leu Val Tyr Ser Asn Lys Cys Gln Thr Pro Leu Gly Met
 1140 1145 1150
 Ala Ser Gly His Ile Arg Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr
 1155 1160 1165
 Gly Gln Trp Ala Pro Lys Leu Ala Arg Leu His Tyr Ser Gly Ser Ile
 1170 1175 1180
 Asn Ala Trp Ser Thr Lys Glu Pro Phe Ser Trp Ile Lys Val Asp Leu
 1185 1190 1195 1200
 Leu Ala Pro Met Ile Ile His Gly Ile Lys Thr Gln Gly Ala Arg Gln
 1205 1210 1215
 Lys Phe Ser Ser Leu Tyr Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu
 1220 1225 1230
 Asp Gly Lys Lys Trp Gln Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu
 1235 1240 1245
 Met Val Phe Phe Gly Asn Val Asp Ser Ser Gly Ile Lys His Asn Ile
 1250 1255 1260
 Phe Asn Pro Pro Ile Ile Ala Arg Tyr Ile Arg Leu His Pro Thr His
 1265 1270 1275 1280
 Tyr Ser Ile Arg Ser Thr Leu Arg Met Glu Leu Met Gly Cys Asp Leu
 1285 1290 1295
 Asn Ser Cys Ser Met Pro Leu Gly Met Glu Ser Lys Ala Ile Ser Asp
 1300 1305 1310
 Ala Gln Ile Thr Ala Ser Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp
 1315 1320 1325
 Ser Pro Ser Lys Ala Arg Leu His Leu Gln Gly Arg Ser Asn Ala Trp
 1330 1335 1340
 Arg Pro Gln Val Asn Asn Pro Lys Glu Trp Leu Gln Val Asp Phe Gln
 1345 1350 1355 1360
 Lys Thr Met Lys Val Thr Gly Val Thr Thr Gln Gly Val Lys Ser Leu
 1365 1370 1375
 Leu Thr Ser Met Tyr Val Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp
 1380 1385 1390
 Gly His Gln Trp Thr Leu Phe Phe Gln Asn Gly Lys Val Lys Val Phe
 1395 1400 1405
 Gln Gly Asn Gln Asp Ser Phe Thr Pro Val Val Asn Ser Leu Asp Pro
 1410 1415 1420

Pro Leu Leu Thr Arg Tyr Leu Arg Ile His Pro Gln Ser Trp Val His
 1425 1430 1435 1440
 Gln Ile Ala Leu Arg Met Glu Val Leu Gly Cys Glu Ala Gln Asp Leu
 1445 1450 1455
 Tyr .

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<210> 18
<211> 4401
<212> DNA
<213> Artificial Sequence

<220>
<223> hybrid human and porcine factor VIII sequence

<221> CDS
<222> (1)...(4401)
<223> HP47/OL -- factor VIII having the following
domains: A1p-A2h-app-A3p-C1h-C2h

<400> 18
atg cag cta gag ctc tcc acc tgt gtc ttt ctg tgt ctc ttg cca ctc 48
Met Gln Leu Glu Leu Ser Thr Cys Val Phe Leu Cys Leu Leu Pro Leu
1 5 10 15

ggc ttt agt gcc atc agg aga tac tac ctg ggc gca gtg gaa ctg tcc 96
Gly Phe Ser Ala Ile Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser
20 25 30

tgg gac tac cgg caa agt gaa ctc ctc cgt gag ctg cac gtg gac acc 144
Trp Asp Tyr Arg Gln Ser Glu Leu Leu Arg Glu Leu His Val Asp Thr
35 40 45

aga ttt cct gct aca gcg cca gga gct ctt ccg ttg ggc ccg tca gtc 192
Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val
50 55 60

ctg tac aaa aag act gtg ttc gta gag ttc acg gat caa ctt ttc agc 240
Leu Tyr Lys Lys Thr Val Phe Val Glu Phe Thr Asp Gln Leu Phe Ser
65 70 75 80

gtt gcc agg ccc agg cca cca tgg atg ggt ctg ctg ggt cct acc atc 288
Val Ala Arg Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile
85 90 95

cag gct gag gtt tac gac acg gtg gtc gtt acc ctg aag aac atg gct 336
Gln Ala Glu Val Tyr Asp Thr Val Val Val Thr Leu Lys Asn Met Ala
100 105 110

tct cat ccc gtt agt ctt cac gct gtc ggc gtc tcc ttc tgg aaa tct 384
Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Phe Trp Lys Ser
115 120 125

tcc gaa ggc gct gaa tat gag gat cac acc agc caa agg gag aag gaa 432
Ser Glu Gly Ala Glu Tyr Glu Asp His Thr Ser Gln Arg Glu Lys Glu
130 135 140

gac gat aaa gtc ctt ccc ggt aaa agc caa acc tac gtc tgg cag gtc 480
Asp Asp Lys Val Leu Pro Gly Lys Ser Gln Thr Tyr Val Trp Gln Val
145 150 155 160

ctg aaa gaa aat ggt cca aca gcc tct gac cca cca tgt ctt acc tac 528
Leu Lys Glu Asn Gly Pro Thr Ala Ser Asp Pro Pro Cys Leu Thr Tyr
165 170 175

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tca tac ctg tct cac gtg gac ctg gtg aaa gac ctg aat tcg ggc ctc Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu 180 185 190	576
att gga gcc ctg ctg gtt tgt aga gaa ggg agt ctg acc aga gaa agg Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Thr Arg Glu Arg 195 200 205	624
acc cag aac ctg cac gaa ttt gta cta ctt ttt gct gtc ttt gat gaa Thr Gln Asn Leu His Glu Phe Val Leu Leu Phe Ala Val Phe Asp Glu 210 215 220	672
ggg aaa agt tgg cac tca gca aga aat gac tcc tgg aca cgg gcc atg Gly Lys Ser Trp His Ser Ala Arg Asn Asp Ser Trp Thr Arg Ala Met 225 230 235 240	720
gat ccc gca cct gcc agg gcc cag cct gca atg cac aca gtc aat ggc Asp Pro Ala Pro Ala Arg Ala Gln Pro Ala Met His Thr Val Asn Gly 245 250 255	768
tat gtc aac agg tct ctg cca ggt ctg atc gga tgt cat aag aaa tca Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Lys Ser 260 265 270	816
gtc tac tgg cac gtg att gga atg ggc acc agc ccg gaa gtg cac tcc Val Tyr Trp His Val Ile Gly Met Gly Thr Ser Pro Glu Val His Ser 275 280 285	864
att ttt ctt gaa ggc cac acg ttt ctc gtg agg cac cat cgc cag gct Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg His His Arg Gln Ala 290 295 300	912
tcc ttg gag atc tcg cca cta act ttc ctc act gct cag aca ttc ctg Ser Leu Glu Ile Ser Pro Leu Thr Phe Leu Ala Gln Thr Phe Leu 305 310 315 320	960
atg gac ctt ggc cag ttc cta ctg ttt tgt cat atc tct tcc cac cac Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His His 325 330 335	1008
cat ggt ggc atg gag gct cac gtc aga gta gaa agc tgc gcc gag gag His Gly Gly Met Glu Ala His Val Arg Val Glu Ser Cys Ala Glu Glu 340 345 350	1056
ccc cag ctg cgg agg aaa gct gat gaa gag gaa gat tat gat gac aat Pro Gln Leu Arg Arg Lys Ala Asp Glu Glu Asp Tyr Asp Asp Asn 355 360 365	1104
ttg tac gac tcg gac atg gac gtc gtc cgg ctc gat ggt gac gac gtg Leu Tyr Asp Ser Asp Met Asp Val Val Arg Leu Asp Gly Asp Asp Val 370 375 380	1152
tct ccc ttt atc caa atc cgc tca gtt gcc aag aag cat cct aaa act Ser Pro Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr 385 390 395 400	1200
tgg gta cat tac att gct gct gaa gag gag gac tgg gac tat gct ccc Trp Val His Tyr Ile Ala Ala Glu Glu Asp Trp Asp Tyr Ala Pro 405 410 415	1248
tta gtc ctc gcc ccc gat gac aga agt tat aaa agt caa tat ttg aac Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn 420 425 430	1296
aat ggc cct cag cgg att ggt agg aag tac aaaa aaa gtc cga ttt atg Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met	1344

435

440

445

gca tac aca gat gaa acc ttt aag acg cgt gaa gct att cag cat gaa			1392
Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu			
450	455	460	
tca gga atc ttg gga cct tta ctt tat ggg gaa gtt gga gac aca ctg			1440
Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu			
465	470	475	480
ttg att ata ttt aag aat caa gca agc aga cca tat aac atc tac cct			1488
Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro			
485	490	495	
cac gga atc act gat gtc cgt cct ttg tat tca agg aga tta cca aaa			1536
His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys			
500	505	510	
ggt gta aaa cat ttg aag gat ttt cca att ctg cca gga gaa ata ttc			1584
Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe			
515	520	525	
aaa tat aaa tgg aca gtg act gta gaa gat ggg cca act aaa tca gat			1632
Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp			
530	535	540	
ccg cgg tgc ctg acc cgc tat tac tct agt ttc gtt aat atg gag aga			1680
Pro Arg Cys Leu Thr Arg Tyr Ser Ser Phe Val Asn Met Glu Arg			
545	550	555	560
gat cta gct tca gga ctc att ggc cct ctc atc tgc tac aaa gaa			1728
Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu			
565	570	575	
tct gta gat caa aga gga aac cag ata atg tca gac aag agg aat gtc			1776
Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val			
580	585	590	
atc ctg ttt tct gta ttt gat gag aac cga agc tgg tac ctc aca gag			1824
Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu			
595	600	605	
aat ata caa cgc ttt ctc ccc aat cca gct gga gtg cag ctt gag gat			1872
Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp			
610	615	620	
cca gag ttc caa gcc tcc aac atc atg cac agc atc aat ggc tat gtt			1920
Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val			
625	630	635	640
ttt gat agt ttg cag ttg tca gtt tgt ttg cat gag gtg gca tac tgg			1968
Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp			
645	650	655	
tac att cta agc att gga gca cag act gac ttc ctt tct gtc ttc ttc			2016
Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe			
660	665	670	
tct gga tat acc ttc aaa cac aaa atg gtc tat gaa gac aca ctc acc			2064
Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr			
675	680	685	
cta ttc cca ttc tca gga gaa act gtc ttc atg tcg atg gaa aac cca			2112
Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro			
690	695	700	

ggt cta tgg att ctg ggg tgc cac aac tca gac ttt cgg aac aga ggc Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly 705 710 715 720	2160
atg acc gcc tta ctg aag gtt tct agt tgt gac aag aac act ggt gat Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp 725 730 735	2208
tat tac gag gac agt tat gaa gat att tca gca tac ttg ctg agt aaa Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys 740 745 750	2256
aac aat gcc att gaa cct agg agc ttt gcc cag aat tca aga ccc cct Asn Asn Ala Ile Glu Pro Arg Ser Phe Ala Gln Asn Ser Arg Pro Pro 755 760 765	2304
agt gcg agc gct cca aag cct ccg gtc ctg cga cgg cat cag agg gac Ser Ala Ser Ala Pro Lys Pro Pro Val Leu Arg Arg His Gln Arg Asp 770 775 780	2352
ata agc ctt cct act ttt cag ccg gag gaa gac aaa atg gac tat gat Ile Ser Leu Pro Thr Phe Gln Pro Glu Glu Asp Lys Met Asp Tyr Asp 785 790 795 800	2400
gat atc ttc tca act gaa acg aag gga gaa gat ttt gac att tac ggt Asp Ile Phe Ser Thr Glu Thr Lys Gly Glu Asp Phe Asp Ile Tyr Gly 805 810 815	2448
gag gat gaa aat cag gac cct cgc agc ttt cag aag aga acc cga cac Glu Asp Glu Asn Gln Asp Pro Arg Ser Phe Gln Lys Arg Thr Arg His 820 825 830	2496
tat ttc att gct gcg gtg gag cag ctc tgg gat tac ggg atg agc gaa Tyr Phe Ile Ala Ala Val Glu Gln Leu Trp Asp Tyr Gly Met Ser Glu 835 840 845	2544
tcc ccc cgg qcg cta aga aac agg gct cag aac gga gag gtg cct cgg Ser Pro Arg Ala Leu Arg Asn Arg Ala Gln Asn Gly Glu Val Pro Arg 850 855 860	2592
ttc aag aag gtg gtc ttc cgg gaa ttt gct gac ggc tcc ttc acg cag Phe Lys Lys Val Val Phe Arg Glu Phe Ala Asp Gly Ser Phe Thr Gln 865 870 875 880	2640
ccg tcg tac cgc ggg gaa ctc aac aaa cac ttg ggg ctc ttg gga ccc Pro Ser Tyr Arg Gly Glu Leu Asn Lys His Leu Gly Leu Leu Gly Pro 885 890 895	2688
tac atc aga gcg gaa gtt gaa gac aac atc atg gta act ttc aaa aac Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val Thr Phe Lys Asn 900 905 910	2736
cag gcg tct cgt ccc tat tcc ttc tac tcg agc ctt att tct tat ccg Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Pro 915 920 925	2784
gat gat cag gag caa ggg gca gaa cct cga cac aac ttc gtc cag cca Asp Asp Gln Glu Gln Gly Ala Glu Pro Arg His Asn Phe Val Gln Pro 930 935 940	2832
aat gaa acc aga act tac ttt tgg aaa gtg cag cat cac atg gca ccc Asn Glu Thr Arg Thr Tyr Phe Trp Lys Val Gln His His Met Ala Pro 945 950 955 960	2880
aca gaa gac gag ttt gac tgc aaa gcc tgg gcc tac ttt tct gat gtt Thr Glu Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val	2928

965	970	975	
gac ctg gaa aaa gat gtg cac tca ggc ttg atc ggc ccc ctt ctg atc Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly Pro Leu Leu Ile 980	985	990	2976
tgc cgc gcc aac acc ctg aac gct gct cac ggt aga caa gtg acc acc gtg Cys Arg Ala Asn Thr Leu Asn Ala Ala His Gly Arg Gln Val Thr Val 995	1000	1005	3024
caa gaa ttt gct ctg ttt ttc act att ttt gat gag aca aag agc tgg Gln Glu Phe Ala Leu Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp 1010	1015	1020	3072
tac ttc act gaa aat gtg gaa agg aac tgc cgg gcc ccc tgc cat ctg Tyr Phe Thr Glu Asn Val Glu Arg Asn Cys Arg Ala Pro Cys His Leu 1025	1030	1035	3120
cag atg gag gac ccc act ctg aaa gaa aac tat cgc ttc cat gca atc Gln Met Glu Asp Pro Thr Leu Lys Glu Asn Tyr Arg Phe His Ala Ile 1045	1050	1055	3168
aat ggc tat gtg atg gat aca ctc cct ggc tta gta atg gct cag aat Asn Gly Tyr Val Met Asp Thr Leu Pro Gly Leu Val Met Ala Gln Asn 1060	1065	1070	3216
caa agg atc cga tgg tat ctg ctc agc atg ggc agc aat gaa aat atc Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn Ile 1075	1080	1085	3264
cat tcg att cat ttt agc gga cac gtg ttc agt gta cgg aaa aag gag His Ser Ile His Phe Ser Gly His Val Phe Ser Val Arg Lys Lys Glu 1090	1095	1100	3312
gag tat aaa atg gcc gtg tac aat ctc tat ccg ggt gtc ttt gag aca Glu Tyr Lys Met Ala Val Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr 1105	1110	1115	3360
gtg gaa atg cta ccg tcc aaa gtt gga att tgg cga ata gaa tgc ctg Val Glu Met Leu Pro Ser Lys Val Gly Ile Trp Arg Ile Glu Cys Leu 1125	1130	1135	3408
att ggc gag cac ctg caa gct ggg atg agc acg act ttc ctg gtg tac Ile Gly Glu His Leu Gln Ala Gly Met Ser Thr Thr Phe Leu Val Tyr 1140	1145	1150	3456
agc aag aag tgt cag act ccc ctg gga atg gct tct gga cac att aga Ser Lys Lys Cys Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile Arg 1155	1160	1165	3504
gat ttt cag att aca gct tca gga caa tat gga cag tgg gcc cca aag Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys 1170	1175	1180	3552
ctg gcc aga ctt cat tat tcc gga tca atc aat gcc tgg agc acc aag Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys 1185	1190	1195	3600
gag ccc ttt tct tgg atc aag gtg gat ctg ttg gca cca atg att att Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile 1205	1210	1215	3648
cac ggc atc aag acc cag ggt gcc cgt cag aag ttc tcc agc ctc tac His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr 1220	1225	1230	3696

atc tct cag ttt atc atc atg tat agt ctt gat ggg aag aag tgg cag Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln 1235 1240 1245	3744
act tat cga gga aat tcc act gga acc tta atg gtc ttc ttt ggc aat Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn 1250 1255 1260	3792
gtg gat tca tct ggg ata aaa cac aat att ttt aac cct cca att att Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Ile 1265 1270 1275 1280	3840
gct cga tac atc cgt ttg cac cca act cat tat agc att cgc agc act Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr 1285 1290 1295	3888
ctt cgc atg gag ttg atg ggc tgt gat tta aat agt tgc agc atg cca Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro 1300 1305 1310	3936
ttg gga atg gag agt aaa gca ata tca gat gca cag att act gct tca Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr Ala Ser 1315 1320 1325	3984
tcc tac ttt acc aat atg ttt gcc acc tgg tct cct tca aaa gct cga Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg 1330 1335 1340	4032
ctt cac ctc caa ggg agg agt aat gcc tgg aga cct cag gtg aat aat Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn Asn 1345 1350 1355 1360	4080
cca aaa gag tgg ctg caa gtg gac ttc cag aag aca atg aaa gtc aca Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val Thr 1365 1370 1375	4128
gga gta act act cag gga gta aaa tct ctg ctt acc agc atg tat gtg Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr Ser Met Tyr Val 1380 1385 1390	4176
aag gag ttc ctc atc tcc agc agt caa gat ggc cat cag tgg act ctc Lys Glu Phe Leu Ile Ser Ser Gln Asp Gly His Gln Trp Thr Leu 1395 1400 1405	4224
ttt ttt cag aat ggc aaa gta aag gtt ttt cag gga aat caa gac tcc Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Gln Asp Ser 1410 1415 1420	4272
ttc aca cct gtg gtg aac tct cta gac cca ccg tta ctg act cgc tac Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr 1425 1430 1435 1440	4320
ctt cga att cac ccc cag agt tgg gtg cac cag att gcc ctg agg atg Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg Met 1445 1450 1455	4368
gag gtt ctg ggc tgc gag gca cag gac ctc tac Glu Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr 1460 1465	4401

<210> 19
 <211> 1467
 <212> PRT
 <213> Artificial Sequence

<220>

<223> HP47/OL -- factor VIII having the following
domains: A1p-A2h-app-A3p-C1h-C2h

<400> 19

Met Gln Leu Glu Leu Ser Thr Cys Val Phe Leu Cys Leu Leu Pro Leu
1 5 10 15
Gly Phe Ser Ala Ile Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser
20 25 30
Trp Asp Tyr Arg Gln Ser Glu Leu Leu Arg Glu Leu His Val Asp Thr
35 40 45
Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val
50 55 60
Leu Tyr Lys Lys Thr Val Phe Val Glu Phe Thr Asp Gln Leu Phe Ser
65 70 75 80
Val Ala Arg Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile
85 90 95
Gln Ala Glu Val Tyr Asp Thr Val Val Val Thr Leu Lys Asn Met Ala
100 105 110
Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Phe Trp Lys Ser
115 120 125
Ser Glu Gly Ala Glu Tyr Glu Asp His Thr Ser Gln Arg Glu Lys Glu
130 135 140
Asp Asp Lys Val Leu Pro Gly Lys Ser Gln Thr Tyr Val Trp Gln Val
145 150 155 160
Leu Lys Glu Asn Gly Pro Thr Ala Ser Asp Pro Pro Cys Leu Thr Tyr
165 170 175
Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu
180 185 190
Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Thr Arg Glu Arg
195 200 205
Thr Gln Asn Leu His Glu Phe Val Leu Leu Phe Ala Val Phe Asp Glu
210 215 220
Gly Lys Ser Trp His Ser Ala Arg Asn Asp Ser Trp Thr Arg Ala Met
225 230 235 240
Asp Pro Ala Pro Ala Arg Ala Gln Pro Ala Met His Thr Val Asn Gly
245 250 255
Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Lys Lys Ser
260 265 270
Val Tyr Trp His Val Ile Gly Met Gly Thr Ser Pro Glu Val His Ser
275 280 285
Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg His His Arg Gln Ala
290 295 300
Ser Leu Glu Ile Ser Pro Leu Thr Phe Leu Thr Ala Gln Thr Phe Leu
305 310 315 320
Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His His
325 330 335
His Gly Gly Met Glu Ala His Val Arg Val Glu Ser Cys Ala Glu Glu
340 345 350
Pro Gln Leu Arg Arg Lys Ala Asp Glu Glu Asp Tyr Asp Asp Asn
355 360 365
Leu Tyr Asp Ser Asp Met Asp Val Val Arg Leu Asp Gly Asp Asp Val
370 375 380
Ser Pro Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr
385 390 395 400
Trp Val His Tyr Ile Ala Ala Glu Glu Asp Trp Asp Tyr Ala Pro
405 410 415
Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn
420 425 430
Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met
435 440 445
Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu
450 455 460
Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu
465 470 475 480
Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro

485	490	495
His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg	Leu Pro Lys	
500	505	510
Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro	Gly Glu Ile Phe	
515	520	525
Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro	Thr Lys Ser Asp	
530	535	540
Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser	Phe Val Asn Met Glu Arg	
545	550	560
Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile	Cys Tyr Lys Glu	
565	570	575
Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp	Lys Arg Asn Val	
580	585	590
Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp	Tyr Leu Thr Glu	
595	600	605
Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val	Gln Leu Glu Asp	
610	615	620
Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile	Asn Gly Tyr Val	
625	630	635
Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu	Val Ala Tyr Trp	
645	650	655
Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu	Ser Val Phe Phe	
660	665	670
Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu	Asp Thr Leu Thr	
675	680	685
Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser	Met Glu Asn Pro	
690	695	700
Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe	Arg Asn Arg Gly	
705	710	715
Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys	Asn Thr Gly Asp	
725	730	735
Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala	Tyr Leu Leu Ser Lys	
740	745	750
Asn Asn Ala Ile Glu Pro Arg Ser Phe Ala Gln Asn	Ser Arg Pro Pro	
755	760	765
Ser Ala Ser Ala Pro Lys Pro Pro Val Leu Arg Arg	His Gln Arg Asp	
770	775	780
Ile Ser Leu Pro Thr Phe Gln Pro Glu Glu Asp Lys	Met Asp Tyr Asp	
785	790	795
Asp Ile Phe Ser Thr Glu Thr Lys Gly Glu Asp Phe	Asp Ile Tyr Gly	
805	810	815
Glu Asp Glu Asn Gln Asp Pro Arg Ser Phe Gln Lys	Arg Thr Arg His	
820	825	830
Tyr Phe Ile Ala Ala Val Glu Gln Leu Trp Asp Tyr	Gly Met Ser Glu	
835	840	845
Ser Pro Arg Ala Leu Arg Asn Arg Ala Gln Asn	Gly Glu Val Pro Arg	
850	855	860
Phe Lys Lys Val Val Phe Arg Glu Phe Ala Asp Gly	Ser Phe Thr Gln	
865	870	875
Pro Ser Tyr Arg Gly Glu Leu Asn Lys His Leu	Gly Leu Leu Gly Pro	
885	890	895
Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val	Thr Phe Lys Asn	
900	905	910
Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser	Leu Ile Ser Tyr Pro	
915	920	925
Asp Asp Gln Glu Gln Gly Ala Glu Pro Arg His Asn	Phe Val Gln Pro	
930	935	940
Asn Glu Thr Arg Thr Tyr Phe Trp Lys Val Gln His	His His Met Ala Pro	
945	950	960
Thr Glu Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr	Phe Ser Asp Val	
965	970	975
Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly	Pro Leu Leu Ile	
980	985	990
Cys Arg Ala Asn Thr Leu Asn Ala Ala His Gly Arg	Gln Val Thr Val	
995	1000	1005
Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe Asp Glu	Thr Lys Ser Trp	

1010	1015	1020
Tyr Phe Thr Glu Asn Val Glu Arg Asn Cys Arg Ala Pro Cys His Leu		
1025	1030	1035
Gln Met Glu Asp Pro Thr Leu Lys Glu Asn Tyr Arg Phe His Ala Ile		1040
1045	1050	1055
Asn Gly Tyr Val Met Asp Thr Leu Pro Gly Leu Val Met Ala Gln Asn		
1060	1065	1070
Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn Ile		
1075	1080	1085
His Ser Ile His Phe Ser Gly His Val Phe Ser Val Arg Lys Lys Glu		
1090	1095	1100
Glu Tyr Lys Met Ala Val Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr		
1105	1110	1115
Val Glu Met Leu Pro Ser Lys Val Gly Ile Trp Arg Ile Glu Cys Leu		1120
1125	1130	1135
Ile Gly Glu His Leu Gln Ala Gly Met Ser Thr Thr Phe Leu Val Tyr		
1140	1145	1150
Ser Lys Lys Cys Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile Arg		
1155	1160	1165
Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys		
1170	1175	1180
Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys		
1185	1190	1195
Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Ala Pro Met Ile Ile		1200
1205	1210	1215
His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr		
1220	1225	1230
Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln		
1235	1240	1245
Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn		
1250	1255	1260
Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Ile		
1265	1270	1275
Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr		
1285	1290	1295
Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro		
1300	1305	1310
Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr Ala Ser		
1315	1320	1325
Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg		
1330	1335	1340
Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn Asn		
1345	1350	1355
Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val Thr		1360
1365	1370	1375
Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr Ser Met Tyr Val		
1380	1385	1390
Lys Glu Phe Leu Ile Ser Ser Gln Asp Gly His Gln Trp Thr Leu		
1395	1400	1405
Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Gln Asp Ser		
1410	1415	1420
Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr		
1425	1430	1435
Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg Met		1440
1445	1450	1455
Glu Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr		
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<211> 4401

<212> DNA

<213> Artificial Sequence

<220>

<223> hybrid human and porcine factor VIII sequence

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Met Gln Leu Glu Leu Ser Thr Cys Val Phe Leu Cys Leu Leu Pro Leu
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ggc ttt agt gcc atc agg aga tac tac ctg ggc gca gtg gaa ctg tcc 96
Gly Phe Ser Ala Ile Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser
20 25 30

tgg gac tac cgg caa agt gaa ctc ctc cgt gag ctg cac gtg gac acc 144
Trp Asp Tyr Arg Gln Ser Glu Leu Leu Arg Glu Leu His Val Asp Thr
35 40 45

aga ttt cct gct aca gcg cca gga gct ctt ccg ttg ggc ccg tca gtc 192
Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val
50 55 60

ctg tac aaa aag act gtg ttc gta gag ttc acg gat caa ctt ttc agc 240
Leu Tyr Lys Lys Thr Val Phe Val Glu Phe Thr Asp Gln Leu Phe Ser
65 70 75 80

gtt gcc agg ccc agg cca cca tgg atg ggt ctg ctg ggt cct acc atc 288
Val Ala Arg Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile
85 90 95

cag gct gag gtt tac gac acg gtg gtc gtt acc ctg aag aac atg gct 336
Gln Ala Glu Val Tyr Asp Thr Val Val Val Thr Leu Lys Asn Met Ala
100 105 110

tct cat ccc gtt agt ctt cac gct gtc ggc gtc tcc ttc tgg aaa tct 384
Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Phe Trp Lys Ser
115 120 125

tcc gaa ggc gct gaa tat gag gat cac acc agc caa agg gag aag gaa 432
Ser Glu Gly Ala Glu Tyr Glu Asp His Thr Ser Gln Arg Glu Lys Glu
130 135 140

gac gat aaa gtc ctt ccc ggt aaa agc caa acc tac gtc tgg cag gtc 480
Asp Asp Lys Val Leu Pro Gly Lys Ser Gln Thr Tyr Val Trp Gln Val
145 150 155 160

ctg aaa gaa aat ggt cca aca gcc tct gac cca cca tgt ctt acc tac 528
Leu Lys Glu Asn Gly Pro Thr Ala Ser Asp Pro Pro Cys Leu Thr Tyr
165 170 175

tca tac ctg tct cac gtg gac ctg gtg aaa gac ctg aat tcg ggc ctc 576
Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu
180 185 190

att gga gcc ctg ctg gtt tgt aga gaa ggg agt ctg acc aga gaa agg 624
Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Thr Arg Glu Arg
195 200 205

acc cag aac ctg cac gaa ttt gta cta ctt ttt gct gtc ttt gat gaa 672
Thr Gln Asn Leu His Glu Phe Val Leu Leu Phe Ala Val Phe Asp Glu
210 215 220

ggg aaa agt tgg cac tca gca aga aat gac tcc tgg aca cgg gcc atg 720
Gly Lys Ser Trp His Ser Ala Arg Asn Asp Ser Trp Thr Arg Ala Met
225 230 235 240

gat ccc gca cct gcc agg gcc cag cct gca atg cac aca gtc aat ggc	768
Asp Pro Ala Pro Ala Arg Ala Gln Pro Ala Met His Thr Val Asn Gly	
245 250 255	
tat gtc aac agg tct ctg cca ggt ctg atc gga tgt cat aag aaa tca	816
Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Lys Lys Ser	
260 265 270	
gtc tac tgg cac gtg att gga atg ggc acc agc ccg gaa gtg cac tcc	864
Val Tyr Trp His Val Ile Gly Met Gly Thr Ser Pro Glu Val His Ser	
275 280 285	
att ttt ctt gaa ggc cac acg ttt ctc gtg agg cac cat cgc cag gct	912
Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg His His Arg Gln Ala	
290 295 300	
tcc ttg gag atc tcg cca cta act ttc ctc act gct cag aca ttc ctg	960
Ser Leu Glu Ile Ser Pro Leu Thr Phe Leu Thr Ala Gln Thr Phe Leu	
305 310 315 320	
atg gac ctt ggc cag ttc cta ctg ttt tgt cat atc tct tcc cac cac	1008
Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His His	
325 330 335	
cat ggt ggc atg gag gct cac gtc aga gta gaa agc tgc gcc gag gag	1056
His Gly Gly Met Glu Ala His Val Arg Val Glu Ser Cys Ala Glu Glu	
340 345 350	
ccc cag ctg cgg agg aaa gct gat gaa gag gaa gat tat gat gac aat	1104
Pro Gln Leu Arg Arg Lys Ala Asp Glu Glu Asp Tyr Asp Asp Asn	
355 360 365	
ttg tac gac tcg gac atg gac gtg gtc cgg ctc gat ggt gac gac gtg	1152
Leu Tyr Asp Ser Asp Met Asp Val Val Arg Leu Asp Gly Asp Asp Val	
370 375 380	
tct ccc ttt atc caa atc cgc tca gtt gcc aag aag cat cct aaa act	1200
Ser Pro Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr	
385 390 395 400	
tgg gta cat tac att gct gct gaa gag gag gac tgg gac tat gct ccc	1248
Trp Val His Tyr Ile Ala Ala Glu Glu Asp Trp Asp Tyr Ala Pro	
405 410 415	
tta gtc ctc gcc ccc gat gac aga agt tat aaa agt caa tat ttg aac	1296
Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn	
420 425 430	
aat ggc cct cag cgg att ggt agg aag tac aaa aaa gtc cga ttt atg	1344
Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met	
435 440 445	
gca tac aca gat gaa acc ttt aag act cgt gaa gct att cag cat gaa	1392
Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu	
450 455 460	
tca gga atc ttg gga cct tta ctt tat ggg gaa gtt gga gac aca ctg	1440
Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu	
465 470 475 480	
ttg att ata ttt aag aat caa gca agc aga cca tat aac atc tac cct	1488
Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro	
485 490 495	
cac gga atc act gat gtc cgt cct ttg tat tca agg aga tta cca aaa	1536
His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys	

500	505	510	
ggt gta aaa cat ttg aag gat ttt cca att ctg cca gga gaa ata ttc Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe 515	520	525	1584
aaa tat aaa tgg aca gtg act gta gaa gat ggg cca act aaa tca gat Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp 530	535	540	1632
cct cgg tgc ctg acc cgc tat tac tct agt ttc gtt aat atg gag aga Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg 545	550	555	1680
gat cta gct tca gga ctc att ggc cct ctc atc tgc tac aaa gaa Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu 565	570	575	1728
tct gta gat caa aga gga aac cag ata atg tca gac aag agg aat gtc Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val 580	585	590	1776
atc ctg ttt tct gta ttt gat gag aac cga agc tgg tac ctc aca gag Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu 595	600	605	1824
aat ata caa cgc ttt ctc ccc aat cca gct gga gtg cag ctt gag gat Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp 610	615	620	1872
cca gag ttc caa gcc tcc aac atc atg cac agc atc aat ggc tat gtt Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val 625	630	635	1920
ttt gat agt ttg cag ttg tca gtt tgt ttg cat gag gtg gca tac tgg Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp 645	650	655	1968
tac att cta agc att gga gca cag act gac ttc ctt tct gtc ttc ttc Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe 660	665	670	2016
tct gga tat acc ttc aaa cac aaa atg gtc tat gaa gac aca ctc acc Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr 675	680	685	2064
cta ttc cca ttc tca gga gaa act gtc ttc atg tcg atg gaa aac cca Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro 690	695	700	2112
ggt cta tgg att ctg ggg tgc cac aac tca gac ttt cgg aac aga ggc Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly 705	710	715	2160
atg acc gcc tta ctg aag gtt tct agt tgt gac aag aac act ggt gat Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp 725	730	735	2208
tat tac gag gac agt tat gaa gat att tca gca tac ttg ctg agt aaa Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys 740	745	750	2256
aac aat gcc att gaa cct agg agc ttc tcc cag aat tca aga cac cct Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Ser Arg His Pro 755	760	765	2304

agc act agg tct caa aac cca cca gtc ttg aaa cgc cat caa cgg gaa Ser Thr Arg Ser Gln Asn Pro Pro Val Leu Lys Arg His Gln Arg Glu 770 775 780	2352
ata act cgt act act ctt cag tca gat caa gag gaa att gac tat gat Ile Thr Arg Thr Thr Leu Gln Ser Asp Gln Glu Glu Ile Asp Tyr Asp 785 790 795 800	2400
gat acc ata tca gtt gaa atg aag aag gaa gat ttt gac att tat gat Asp Thr Ile Ser Val Glu Met Lys Lys Glu Asp Phe Asp Ile Tyr Asp 805 810 815	2448
gag gat gaa aat cag agc ccc cgc agc ttt caa aag aga acc cga cac Glu Asp Glu Asn Gln Ser Pro Arg Ser Phe Gln Lys Arg Thr Arg His 820 825 830	2496
tat ttc att gct gcg gtg gag cag ctc tgg gat tac ggg atg agc gaa Tyr Phe Ile Ala Ala Val Glu Gln Leu Trp Asp Tyr Gly Met Ser Glu 835 840 845	2544
tcc ccc cgg gcg cta aga aac agg gct cag aac gga gag gtg cct cgg Ser Pro Arg Ala Leu Arg Asn Arg Ala Gln Asn Gly Glu Val Pro Arg 850 855 860	2592
ttc aag aag gtg gtc ttc cgg gaa ttt gct gac ggc tcc ttc acg cag Phe Lys Lys Val Val Phe Arg Glu Phe Ala Asp Gly Ser Phe Thr Gln 865 870 875 880	2640
ccg tcg tac cgc ggg gaa ctc aac aaa cac ttg ggg ctc ttg gga ccc Pro Ser Tyr Arg Gly Glu Leu Asn Lys His Leu Gly Leu Leu Gly Pro 885 890 895	2688
tac atc aga gcg gaa gtt gaa gac aac atc atg gta act ttc aaa aac Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val Thr Phe Lys Asn 900 905 910	2736
cag gcg tct cgt ccc tat tcc ttc tac tcg agc ctt att tct tat ccg Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Pro 915 920 925	2784
gat gat cag gag caa ggg gca gaa cct cga aaa aac ttt gtc aag cct Asp Asp Gln Glu Gln Gly Ala Glu Pro Arg Lys Asn Phe Val Lys Pro 930 935 940	2832
aat gaa acc aaa act tac ttt tgg aaa gtg cag cat cac atg gca ccc Asn Glu Thr Lys Thr Tyr Phe Trp Lys Val Gln His His Met Ala Pro 945 950 955 960	2880
aca gaa gac gag ttt gac tgc aaa gcc tgg gcc tac ttt tct gat gtt Thr Glu Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val 965 970 975	2928
gac ctg gaa aaa gat gtg cac tca ggc ttg atc ggc ccc ctt ctg atc Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly Pro Leu Leu Ile 980 985 990	2976
tgc cgc gcc aac acc ctg aac gct gct cac ggt aga caa gtg acc gtg Cys Arg Ala Asn Thr Leu Asn Ala Ala His Gly Arg Gln Val Thr Val 995 1000 1005	3024
caa gaa ttt gct ctg ttt ttc act att ttt gat gag aca aag agc tgg Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp 1010 1015 1020	3072
tac ttc act gaa aat gtg gaa agg aac tgc cgg gcc ccc tgc cat ctg Tyr Phe Thr Glu Asn Val Glu Arg Asn Cys Arg Ala Pro Cys His Leu	3120

1025	1030	1035	1040	
cag atg gag gac ccc act ctg aaa gaa aac tat cgc ttc cat gca atc Gln Met Glu Asp Pro Thr Leu Lys Glu Asn Tyr Arg Phe His Ala Ile				3168
1045		1050	1055	
aat ggc tat gtg atg gat aca ctc cct ggc tta gta atg gct cag aat Asn Gly Tyr Val Met Asp Thr Leu Pro Gly Leu Val Met Ala Gln Asn				3216
1060		1065	1070	
caa agg atc cga tgg tat ctg ctc agc atg ggc agc aat gaa aat atc Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn Ile				3264
1075		1080	1085	
cat tcg att cat ttt agc gga cac gtg ttc agt gta cgg aaa aag gag His Ser Ile His Phe Ser Gly His Val Phe Ser Val Arg Lys Lys Glu				3312
1090		1095	1100	
gag tat aaa atg gcc gtg tac aat ctc tat ccg ggt gtc ttt gag aca Glu Tyr Lys Met Ala Val Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr				3360
1105		1110	1115	1120
gtg gaa atg cta ccg tcc aaa gtt gga att tgg cgg aat aga tgc ctg Val Glu Met Leu Pro Ser Lys Val Gly Ile Trp Arg Asn Arg Cys Leu				3408
1125		1130	1135	
att ggc gag cac ctg caa gct ggg atg agc acg act ttc ctg gtg tac Ile Gly Glu His Leu Gln Ala Gly Met Ser Thr Thr Phe Leu Val Tyr				3456
1140		1145	1150	
agc aag aag tgt cag act ccc ctg gga atg gct tct gga cac att aga Ser Lys Cys Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile Arg				3504
1155		1160	1165	
gat ttt cag att aca gct tca gga caa tat gga cag tgg gcc cca aag Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys				3552
1170		1175	1180	
ctg gcc aga ctt cat tat tcc gga tca atc aat gcc tgg agc acc aag Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys				3600
1185		1190	1195	1200
gag ccc ttt tct tgg atc aag gtg gat ctg ttg gca cca atg att att Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile				3648
1205		1210	1215	
cac ggc atc aag acc cag ggt gcc cgt cag aag ttc tcc agc ctc tac His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr				3696
1220		1225	1230	
atc tct cag ttt atc atc atg tat agt ctt gat ggg aag aag tgg cag Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln				3744
1235		1240	1245	
act tat cga gga aat tcc act gga acc tta atg gtc ttc ttt ggc aat Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn				3792
1250		1255	1260	
gtg gat tca tct ggg ata aaa cac aat att ttt aac cct cca att att Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Ile				3840
1265		1270	1275	1280
gct cga tac atc cgt ttg cac cca act cat tat agc att cgc agc act Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr				3888
1285		1290	1295	

ctt cgc atg gag ttg atg ggc tgc gat tta aat agt tgc agc atg cca Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro 1300 1305 1310	3936
ttg gga atg gag agt aaa gca ata tca gat gca cag att act gct tca Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr Ala Ser 1315 1320 1325	3984
tcc tac ttt acc aat atg ttt gcc acc tgg tct cct tca aaa gct cga Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg 1330 1335 1340	4032
ctt cac ctc caa ggg agg agt aat gcc tgg aga cct cag gtg aat aat Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn Asn 1345 1350 1355 1360	4080
cca aaa gag tgg ctg caa gtg gac ttc cag aag aca atg aaa gtc aca Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val Thr 1365 1370 1375	4128
gga gta act act cag gga gta aaa tct ctg ctt acc agc atg tat gtg Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr Ser Met Tyr Val 1380 1385 1390	4176
aag gag ttc ctc atc tcc agc agt caa gat ggc cat cag tgg act ctc Lys Glu Phe Leu Ile Ser Ser Gln Asp Gly His Gln Trp Thr Leu 1395 1400 1405	4224
ttt ttt cag aat ggc aaa gta aag gtt ttt cag gga aat caa gac tcc Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Gln Asp Ser 1410 1415 1420	4272
ttc aca cct gtg gtg aac tct cta gac cca ccg tta ctg act cgc tac Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr 1425 1430 1435 1440	4320
ctt cga att cac ccc cag agt tgg gtg cac cag att gcc ctg agg atg Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg Met 1445 1450 1455	4368
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<220>
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Gly Phe Ser Ala Ile Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser	
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Trp Asp Tyr Arg Gln Ser Glu Leu Leu Arg Glu Leu His Val Asp Thr	
35 40 45	
Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val	
50 55 60	
Leu Tyr Lys Lys Thr Val Phe Val Glu Phe Thr Asp Gln Leu Phe Ser	
65 70 75 80	
Val Ala Arg Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile	
85 90 95	

Gln Ala Glu Val Tyr Asp Thr Val Val Val Thr Leu Lys Asn Met Ala
 100 105 110
 Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Phe Trp Lys Ser
 115 120 125
 Ser Glu Gly Ala Glu Tyr Glu Asp His Thr Ser Gln Arg Glu Lys Glu
 130 135 140
 Asp Asp Lys Val Leu Pro Gly Lys Ser Gln Thr Tyr Val Trp Gln Val
 145 150 155 160
 Leu Lys Glu Asn Gly Pro Thr Ala Ser Asp Pro Pro Cys Leu Thr Tyr
 165 170 175
 Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu
 180 185 190
 Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Thr Arg Glu Arg
 195 200 205
 Thr Gln Asn Leu His Glu Phe Val Leu Leu Phe Ala Val Phe Asp Glu
 210 215 220
 Gly Lys Ser Trp His Ser Ala Arg Asn Asp Ser Trp Thr Arg Ala Met
 225 230 235 240
 Asp Pro Ala Pro Ala Arg Ala Gln Pro Ala Met His Thr Val Asn Gly
 245 250 255
 Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Lys Lys Ser
 260 265 270
 Val Tyr Trp His Val Ile Gly Met Gly Thr Ser Pro Glu Val His Ser
 275 280 285
 Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg His His Arg Gln Ala
 290 295 300
 Ser Leu Glu Ile Ser Pro Leu Thr Phe Leu Thr Ala Gln Thr Phe Leu
 305 310 315 320
 Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His His
 325 330 335
 His Gly Gly Met Glu Ala His Val Arg Val Glu Ser Cys Ala Glu Glu
 340 345 350
 Pro Gln Leu Arg Arg Lys Ala Asp Glu Glu Asp Tyr Asp Asp Asn
 355 360 365
 Leu Tyr Asp Ser Asp Met Asp Val Val Arg Leu Asp Gly Asp Asp Val
 370 375 380
 Ser Pro Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr
 385 390 395 400
 Trp Val His Tyr Ile Ala Ala Glu Glu Asp Trp Asp Tyr Ala Pro
 405 410 415
 Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn
 420 425 430
 Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met
 435 440 445
 Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu
 450 455 460
 Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu
 465 470 475 480
 Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro
 485 490 495
 His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys
 500 505 510
 Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe
 515 520 525
 Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp
 530 535 540
 Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg
 545 550 555 560
 Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu
 565 570 575
 Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val
 580 585 590
 Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu
 595 600 605
 Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp
 610 615 620

Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val
 625 630 635 640
 Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp
 645 650 655
 Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe
 660 665 670
 Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr
 675 680 685
 Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro
 690 695 700
 Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly
 705 710 715 720
 Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp
 725 730 735
 Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys
 740 745 750
 Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Ser Arg His Pro
 755 760 765
 Ser Thr Arg Ser Gln Asn Pro Pro Val Leu Lys Arg His Gln Arg Glu
 770 775 780
 Ile Thr Arg Thr Thr Leu Gln Ser Asp Gln Glu Glu Ile Asp Tyr Asp
 785 790 795 800
 Asp Thr Ile Ser Val Glu Met Lys Lys Glu Asp Phe Asp Ile Tyr Asp
 805 810 815
 Glu Asp Glu Asn Gln Ser Pro Arg Ser Phe Gln Lys Arg Thr Arg His
 820 825 830
 Tyr Phe Ile Ala Ala Val Glu Gln Leu Trp Asp Tyr Gly Met Ser Glu
 835 840 845
 Ser Pro Arg Ala Leu Arg Asn Arg Ala Gln Asn Gly Glu Val Pro Arg
 850 855 860
 Phe Lys Lys Val Val Phe Arg Glu Phe Ala Asp Gly Ser Phe Thr Gln
 865 870 875 880
 Pro Ser Tyr Arg Gly Glu Leu Asn Lys His Leu Gly Leu Leu Gly Pro
 885 890 895
 Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val Thr Phe Lys Asn
 900 905 910
 Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Pro
 915 920 925
 Asp Asp Gln Glu Gln Gly Ala Glu Pro Arg Lys Asn Phe Val Lys Pro
 930 935 940
 Asn Glu Thr Lys Thr Tyr Phe Trp Lys Val Gln His His Met Ala Pro
 945 950 955 960
 Thr Glu Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val
 965 970 975
 Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly Pro Leu Leu Ile
 980 985 990
 Cys Arg Ala Asn Thr Leu Asn Ala Ala His Gly Arg Gln Val Thr Val
 995 1000 1005
 Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp
 1010 1015 1020
 Tyr Phe Thr Glu Asn Val Glu Arg Asn Cys Arg Ala Pro Cys His Leu
 1025 1030 1035 1040
 Gln Met Glu Asp Pro Thr Leu Lys Glu Asn Tyr Arg Phe His Ala Ile
 1045 1050 1055
 Asn Gly Tyr Val Met Asp Thr Leu Pro Gly Leu Val Met Ala Gln Asn
 1060 1065 1070
 Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn Ile
 1075 1080 1085
 His Ser Ile His Phe Ser Gly His Val Phe Ser Val Arg Lys Lys Glu
 1090 1095 1100
 Glu Tyr Lys Met Ala Val Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr
 1105 1110 1115 1120
 Val Glu Met Leu Pro Ser Lys Val Gly Ile Trp Arg Asn Arg Cys Leu
 1125 1130 1135
 Ile Gly Glu His Leu Gln Ala Gly Met Ser Thr Thr Phe Leu Val Tyr
 1140 1145 1150

Ser Lys Lys Cys Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile Arg
 1155 1160 1165
 Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys
 1170 1175 1180
 Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys
 1185 1190 1195 1200
 Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile
 1205 1210 1215
 His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr
 1220 1225 1230
 Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln
 1235 1240 1245
 Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn
 1250 1255 1260
 Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Ile
 1265 1270 1275 1280
 Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr
 1285 1290 1295
 Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro
 1300 1305 1310
 Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr Ala Ser
 1315 1320 1325
 Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg
 1330 1335 1340
 Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn Asn
 1345 1350 1355 1360
 Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val Thr
 1365 1370 1375
 Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr Ser Met Tyr Val
 1380 1385 1390
 Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His Gln Trp Thr Leu
 1395 1400 1405
 Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Gln Asp Ser
 1410 1415 1420
 Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr
 1425 1430 1435 1440
 Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg Met
 1445 1450 1455
 Glu Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr
 1460 1465